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Mycoses and prac

MYCOSES
AND
PRACTICAL MYCOLOGY

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MYCOSES
AND
PRACTICAL MYCOLOGY

A Handbook for Students and Practitioners

by

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To
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PREFACE

This handbook has been written with the aim of supplying the dermatologist and the general practitioner, as well as the student of tropical medicine, with a concise clinical and practical guide to mycotic affections.

Comprehensive accounts of the mycoses have been attempted with some emphasis on both the clinical and laboratory aspects of diagnosis. A few pathogenic species isolated in Egypt are recorded, and there is a certain proportion of original clinical practical and therapeutic observations.

The botanical side of mycology could not be ignored altogether and, although included in a restricted form, will probably be found helpful towards a better understanding of the correct aetiology of the various infections. For more detailed work, it will be necessary to refer to fuller publications, of which Carroll W. Dodge's ' Medical Mycology ' is an outstanding example. A short chapter on fungicides, fungistatics and media is appended together with some notes on poisonous fungi.

It is hoped that the book will serve its purpose in a field which, unfortunately, is only accorded cursory recognition.

N. G.

Cairo,
May 1948.

FOREWORD

I HAVE been asked to write an introduction to this important work on a subject which has up to now been the Cinderella of modern medicine. For a long time it has been evident that there has been need of a reference work on medical Mycology for practitioners and students, not only in the tropics and sub-tropics, but the world over. By those engaged in the teaching of tropical medicine it has become increasingly realised that Mycology must be included in the curriculum for this course.

Dr. Gohar's book should do more than this; it should give precision to a subject upon which there has existed certain confusion regarding nomenclature as well as regarding identification of many pathogenic fungi. The time is now ripe to place this subject on a sure and scientific foundation and this has been achieved by Dr. Gohar in his concise and profusely illustrated work, so that it is confidently expected that it will meet the needs of many practitioners and eventually exert its influence on the teaching of tropical medicine.

The important aspect of treatment is fully dealt with as is opportune, for there have been some advances in this department during the last decade and dissemination of this knowledge is eminently desirable. All these contingencies have been provided for and it now remains for me to wish this book what it deserves, a long and successful career.

PHILIP MANSON-BAHR.

149, *Harley Street, W.*1.

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ERRATA

PLATE II.—Legend should read "Colony of *Favotrichophyton violaceum.*"
" III.— " " " "Colony of *Epidermophyton persicolor.*"
" IV.— " " " "Colony of *Microsporum canis.*"

CHAPTER I

MYCOLOGY

Origin of Fungi

Life as we know it is represented in the two main kingdoms of animals and plants. There are some living forms, however, that occupy positions in this man-made scheme of classification which manifest affinities for one or both main groups, but cannot be definitely attached to either, and are only alloted their respective places for convenience. The group of fungi is one of these indeterminate organisms. The general view is that they are plants; but on comparison with these, the evidence for the assumption is far from conclusive. Unlike them, they are devoid of chlorophyll, and are thus lacking in the photosynthetic power to convert atmospheric carbon dioxide and water in the presence of sunlight into carbohydrates. But, on the other hand, they resemble plants, with a few exceptions, in possessing a cell-membrane, and in absorbing nutrition in solution by osmosis. Their reproduction, on the whole, is carried out by means of spores, which are analogous to plant seeds, although the latter are multicellular young plants in embryo, while spores can claim no more than apparently undifferentiated contents.

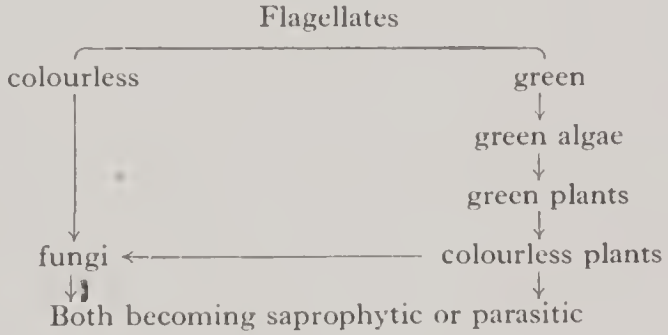
To attempt to settle the exact status of fungi on evolutionary lines is equally abortive. Green plants are considered to have originated from green algae which, in their turn, have had green flagellates as their precursors. The existence of some colourless plants suggests the probability of green ancestors, some of which have lost their chlorophyll and have changed their mode of living into saprophytism or parasitism.

On similar lines of probability, fungi may have arisen from green plants through adaptation and specialization for a new mode of life, or, in another sense, reduction in formerly existing characters with the same end in view. Another hypothesis is that fungi, themselves without chlorophyll, evolved from colourless flagellates related to the green individuals from which algae originated, the evolution being brought about by a desire or necessity to lead a parasitic or saprophytic existence. These arguments are supported by the facts that

green algae, which are chlorophyllous plants bear a close structural resemblance to some fungi, and that both fungi and algae are represented in one unique combination, the least developed group of fungi, the *Phycomycetes* or algal fungi, so termed with the idea that they are degraded algae.

For the sake of convenience fungi are assigned a recognized place in the plant kingdom together with mosses, algae, etc., as *Cryptogams*, reproducing by spores, in contradistinction to the rest, the *Phanerogams* or flowering plants, which reproduce by seeds.

The following scheme shows the probable lines of the evolution of fungi:



There exists also a similarity between some fungi and bacteria. In both chlorophyll is absent, and some species of *Actinomyces* appear on some media in bacillus-like forms. In fact, in some classifications, bacteria and algae are included under fungi in the group *Schizomycetes*.

Definition of Fungi

Fungi may be regarded as degraded plants destitute of chlorophyll, absorbing food already elaborated for them by osmosis from decaying organic matter or from the animal or plant hosts which they parasitize, in some instances living and thriving in total absence of sunlight in the tissue of the host.

Some species of fungi live normally as saprophytes on man and only assume a parasitic nature and become more or less virulent if the resistance of the host is for some reason temporarily lowered. Unlike some animal parasites, they are in no need of intermediate hosts for their transmission; the infection takes place in a direct manner.

Nature is a big reservoir of fungi. Several new species are continuously being reported from man from some tissue or organ. The

fact that there are comparatively few instances of repeated occurrence of the same organism in the same site bears out the theory of their derivation from nature, in which they probably originally existed as saprophytes. Other known species, however, are transmitted to man, through association, from domestic animals, such as dogs, cats, cattle, etc.

The number of fungi which attack by selection one tissue or other and cause diseases with specific symptoms and courses is fairly small; in other words, the cases where one species affects one part of the body only without variation is the exception. In general, an organ or tissue is infected by any one of a big collection of species, invariably producing the same symptoms, morbid condition and course peculiar to the site of infection, more or less irrespective of the aetiologic agents whose effects generally only vary in degree.

Structure of Fungi

Fungi are composed of a *thallus* or vegetative body showing little or no differentiation into leaf, stem or root and a reproductive apparatus. The thallus is a collection of fine filaments known as *hyphae* or *mycelium* of variable diameter, 1μ at most in the *Actinomycetes*, and more in the other groups. A mycelial filament is a mass of protoplasm encased in a cell membrane of unknown composition, probably some form of cellulose similar to chitin. In a few lower fungi the protoplasm is naked.

Two types of mycelium are recognized:

1. *Septate*, represented in the majority of fungi. The protoplasm is divided into cells containing one or more nuclei by means of transverse septa which are often perforated to allow intercommunication between the cells.

2. *Coenocytic*, non-septate (*Phycomycetes*, e.g. *Mucorales*), in which the protoplasm is continuous and multinucleate.

The growth, weaving together and differentiation of the mycelium gives rise to the following structures:

Plectenchyma, hyphae in intertwined groups, held together by some interstitial substance forming a thick tissue.

Prosenchyma, composed of easily recognizable and separable elements.

Pseudoparenchyma, especially found in higher fungi. The hyphae are woven into a dense mass with a tissue-like appearance, the cells dividing in one plane only, e.g. *Ascomycetes* and *Basidiomycetes*.

Hymenium, the fructifying surface, made up of fertile parallel elements and borne of the subhymenial prosenchyma, e.g. hymenium of *Basidiomycetes*.

Fructification, the mycelium surrounding the sexual organs in higher fungi, a reproductive condition.

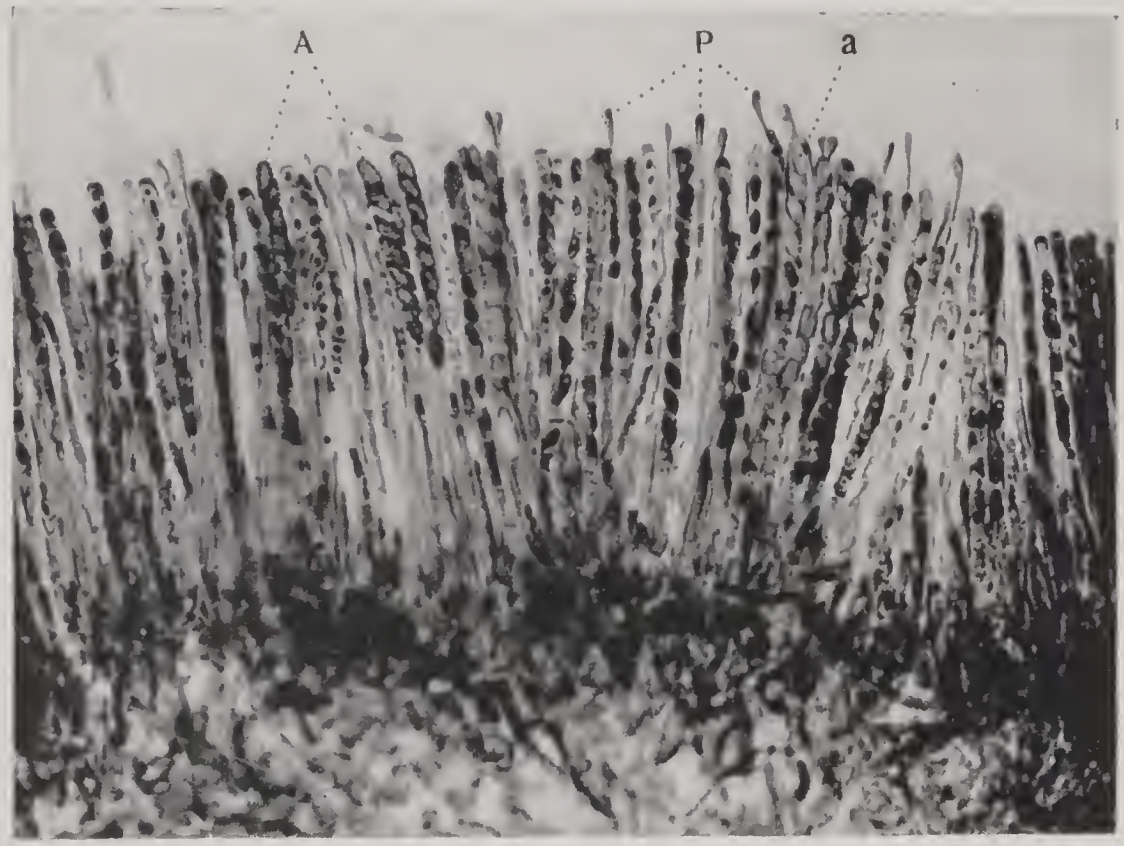


FIG. 1. *Peziza aurantia* (Ascomycetes). Section of hymenium. A. asci, a. ascospore, P. paraphyses. (Original)

Stroma, a plectenchymatous mass, sterile and not involved in any fructification.

Coremium, a group of sexual organs or mycelial filaments bunched together in a bundle, e.g. *Coremium*, *Acremonium*, etc.

Sclerotia, hard tuberiform bodies formed at the end of the vegetative season, with reserve food to tide over adverse conditions, having a plectenchymatous rind and a prosenchymatous core, e.g. ergot of rye, dry cultures of some species of *Aspergillus*.

Bulbil, small sclerotium, occurring in large numbers, formed of a few layers of cells, e.g. the grains of mycetomas.

Rhizoids, tapering root-like hyphae present in saprophytic forms for absorbing nutrition, e.g. *Chytridiales*.

Appressoria, holdfast organs, superficial hyphal branches found in ectoparasites; less often in parasitic forms.

FIG. 2. *Rhizopus niger*. Cultural morphology. c. mushroom-shaped columella after dehiscence of sporangium, s. sporangium, r. rhizoids. (Original)

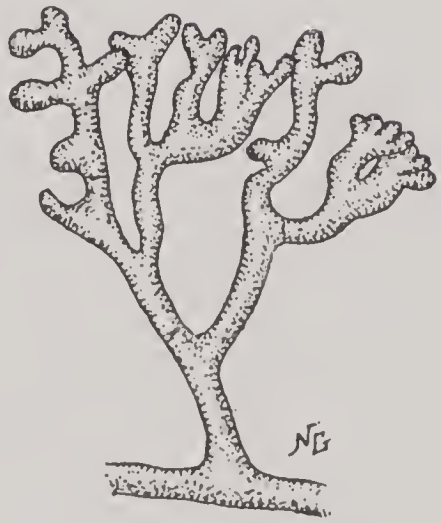


FIG. 3. Appressorium (After R. E. Smith)

Haustoria, blunt coarsely branching hyphae with sucker action penetrating the host for food absorption, found as a rule in parasites on plants.

Sexuality in Fungi

Sexuality manifests itself in nuclear changes in two phases:

1. The *haploid phase*, in which the nucleus contains *n* chromosomes. This is followed by reconstruction of the nucleus at *fertilization*.

2. The *diploid phase*, in which the nucleus contains $2n$ chromosomes and is followed by *meiosis* or reduction division of the nucleus, a return to the *n* chromosome stage.

According as to whether their life-cycles are known or wholly or partially undiscovered, fungi are divided into *perfect forms* and *Fungi Imperfecti* respectively. The latter seem to be able to exist and reproduce without reconstruction of their nuclei. A complete life-cycle in the fungi is, as far as our knowledge goes, the exception.

Reproduction in Fungi

The thallus (vegetative body) may either become wholly or only partially transformed under favourable conditions into a state for assuming reproductive functions. In the former case the fungus is referred to as *holocarpic*, in the latter it is termed *eucarpic*.

The means of reproduction are of two types, *perfect* and *imperfect*. The *perfect type* is seen in the majority of fungi, which group, however, has special characteristics in the form of:

A. *Oospores* or eggs, products of a union between two coenocytic heterogenous gametangia, e.g. *Oomycetes*.

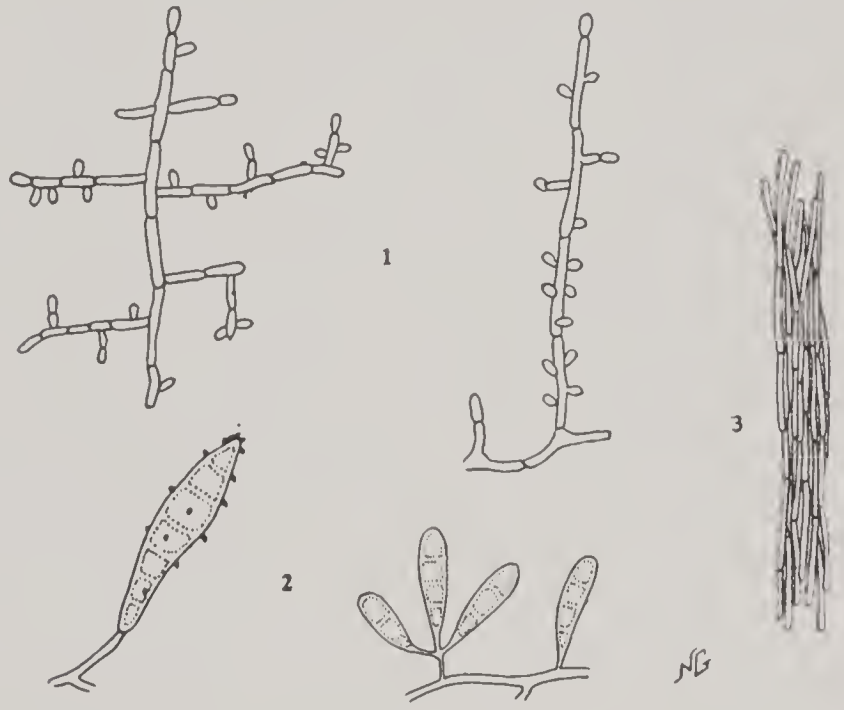


FIG. 4. Septate mycelium. 1. aleurospores (Fr., aleuries), 2. closterospores (Fr., fuseaux), 3. coremium. (Original)

B. *Zygospores*, naked or surrounded by filaments, resulting from the copulation of two isogamous gametangia, e.g. *Zygomycetes* (*Mucoraceae*, *Entomophthoraceae*.)

C. *Ascospores*, develop endogenously in a mother cell called an *ascus*, a sac in which meiosis occurs, containing *n*4 ascospores.

D. *Basidiospores*, exogenously formed on a *basidium*. This type of spore is the main feature in the *Basidiomycetes*, e.g. mushrooms.

The *imperfect type* of reproduction is carried out through accessory and inconstant agencies which do not characterize any one special group of fungi. They take the form of:

A. *Thallospores*:

(*a*) *Arthrospores* or *oidia*, resulting from fragmentation of the mycelium.

(*b*) *Blastospores* or buds, formed by budding of the mycelium.

B. *Aleurospores*, external terminal spores, sessile and single, formed by lateral protoplasmic condensation at the terminations of the hyphae. They are resistant and generally permanent bodies.

C. *Conidia*, exogenous terminal or lateral spores, e.g. in the *Fungi Imperfecti*, easily detachable, hyaline or coloured, occurring singly or in chains, sessile or pedunculated, with a smooth or verrucose surface, non-septate or containing one or more septa. Septate conidia are termed *fuseaux* or *closterospores* if the septation is in one plane, and *muriform* if it happens in three dimensions. Conidia are

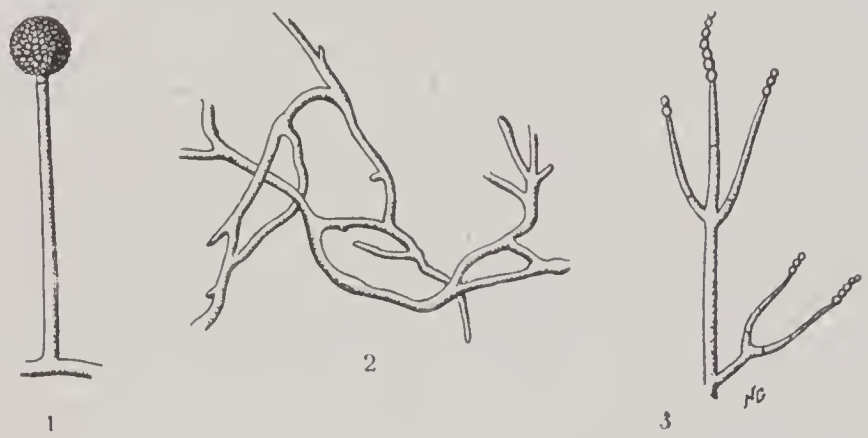


FIG. 5. *Mortierella niveovelutina*. Cultural morphology. 1. sporangiophore and sporangium, 2. complex hyphal anastomoses, 3. aerial conidia (stylospores). (Original)

borne at the tips of specialized stalk-like structures, *sporophores*. When the sporophores produce exogenous spores they are termed *conidiophores*, but sometimes the whole sporophore gets separated by a basal septum from the sterile vegetative mycelium and assumes the shape of a flask which carries the conidia at its extremity and is then known as a *phialide*. A conidiophore is either simple, with or without a phialide, or bundled together with others into a coremium.

D. *Sporangiospores*, formed endogenously in sporophores from specialized cells forming *sporangia*. The sporophores of this type are called *sporangiophores*. A sporangium is formed as a swelling at the tip of the sporangiophore cut off from it by a septum This septum frequently protrudes into the sporangium in a highly convex manner and is termed a *columella*, a feature in the majority of the *Mucorales*.

E. *Chlamydospores*, dormant thick-walled forms to tide over unfavourable periods, arising as condensations of protoplasm either at the ends of hyphae, *terminal*, or at different situations along a hypha,

FIG. 6. *Mucor racemosus*. Cultural morphology. 1. sporangiophores with chlamydospores s. and columella c. with collar, 2 and 3. formation of oidia, 4. chlamydospores. (Original)

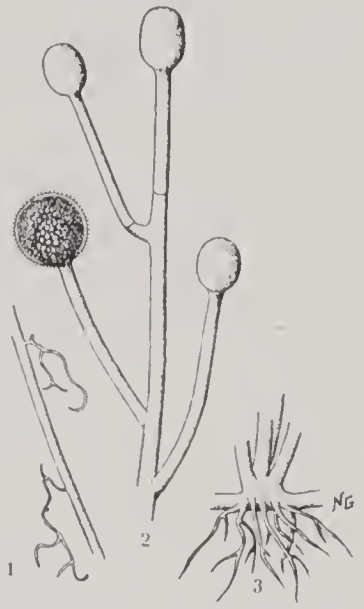
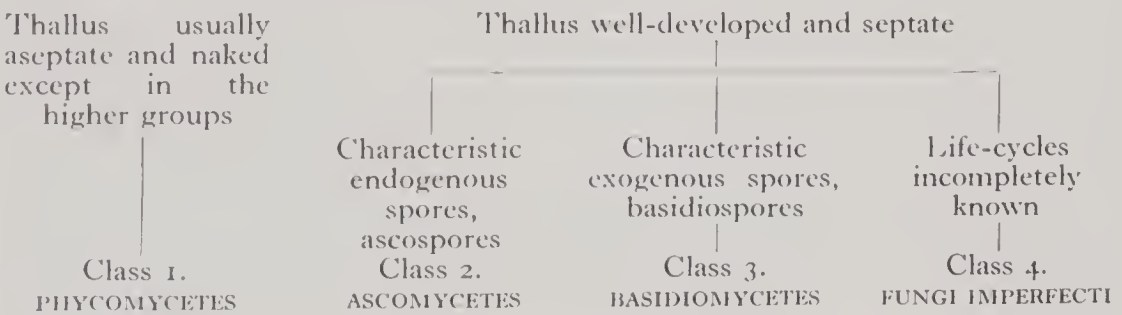


FIG. 7. *Rhizopus parasiticus*. Cultural morphology. 1. septate mycelial filaments with rhizoids, 2. sporangiophores with columella and mature sporangium, 3. sporangiophores and rhizoids opposed to one another arising from a node. (Original)

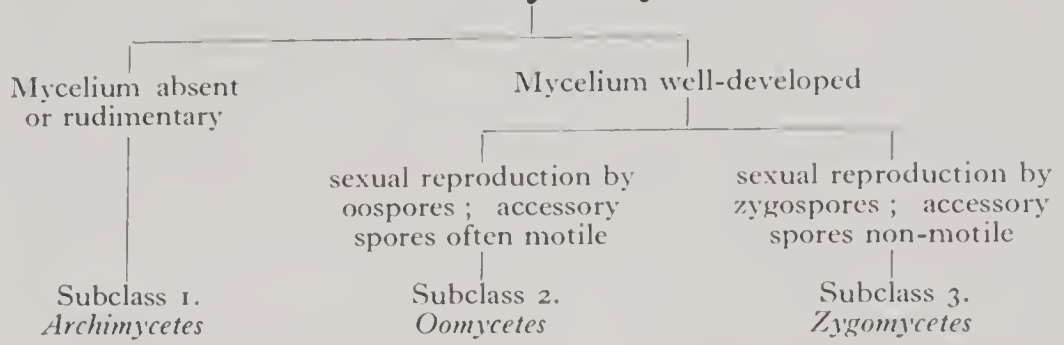
intercalary. Their contents are compact and stain deeply. Strictly speaking, they are asexual spores, inconstant in their appearance.

General Classification of Fungi

Fungi are classified according to the form of the thallus, modes of reproduction and life-cycles. Four classes are recognized and may be identified with the aid of the following scheme. Of these, the *Phycomycetes*, the *Ascomycetes* and the *Hyphomycetes* or *Fungi Imperfecti* are of medical interest.



Class 1. Phycomycetes


Mycelium absent or rudimentary
Mycelium well-developed
sexual reproduction by oospores ; accessory spores often motile
sexual reproduction by zygospores ; accessory spores non-motile
Subclass 1. *Archimycetes*
Subclass 2. *Oomycetes*
Subclass 3. *Zygomycetes*

These are sometimes referred to as algal fungi due to their resemblance to some green algae.

Subclass *Zygomycetes*

Thallus filamentous, coenocytic in the simple forms. Reproduction by means of conidia, non-motile endogenous sporangiospores and by zygospores resulting from the copulation of isogamous gametangia. In higher members, the sporangium may produce mycelium without spore formation. Terrestrial fungi, hence the absence of zoospores. Two orders of the *Zygomycetes* are recognized:

Order 1. *Mucorales*

Terrestrial fungi, generally saprophytes on organic substances, a few are parasites of man and other members of the same group.

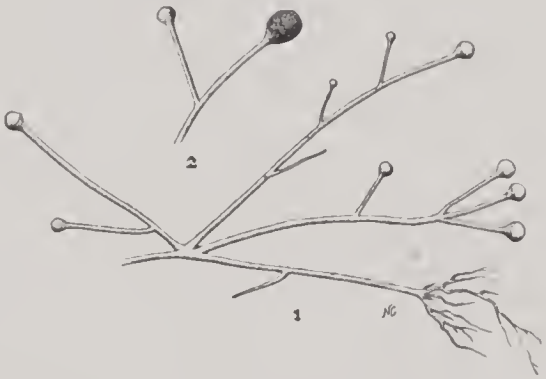


FIG. 8. *Absidia ramosa*. Cultural morphology. Coenocytic mycelium. 1. branching sporangiophores, columellas after dehiscence, and rhizoids, 2. mature sporangium containing the oval sporangiospores and covered with minute crystals of calcium oxalate. (Original)

Order 2. *Entomophthorales*

Mainly parasites of insects and higher fungi.

Class 2. Ascomycetes

Fungi with well-developed branching mycelium of multi- or uninucleate cells, characterized by the production of endogenous

ascospores in specialized sporangia, asci in which meiosis takes place. Conidia of various forms and ascospores are the means of reproduction.

The *Ascomycetes* are divisible into four subclasses:

Subclass 1. ***Hemiascomycetes***

Intermediate in position between *Phycomycetes* and *Ascomycetes*, perithecium lacking, asci naked, free or attached to the extremities of the mycelial filaments, perfect forms, yeasts with ascospores, represented by three orders:

Order 1. Endomycetales

Mycelium generally well-developed, multiplication by transverse division and asci, the direct product of a sexual act, naked, single and well-differentiated from the mycelium. Saprophytes on plants and sugary substances, some are parasites on man.

Order 2. Saccharomycetales

True yeasts with ascospores. Pseudomycelium, no true mycelium, multiplication by budding or by asci which resemble other cells, naked, parasites of man and animals.

Order 3. Exoascales

Asci cylindrical, parallel and non-sheathed, plant parasites.

Subclass 2. ***Plectomycetes***

Ascomycetes with closed and rounded perithecium. They are divided into three orders:

Order 1. Gymnoascales

Some apparently degenerate forms, the dermatophytes of man and animals might possibly belong here.

Order 2. Plectascales

Parasites of man and dead horny substances.

Order 3. Erysiphales

Hymenium in closed perithecium, cause powdery mildew or blight of plants.

Subclass 3. ***Discomycetes***

Ascomycetes with apothecia, hymenium composed of asci and paraphyses. They are divided into five orders which are mainly saprophytic.

Subclass 4. ***Pyrenomycetes***

Ascomycetes with flask-shaped perithecium opening by an ostiole and containing a hymenium with asci, paraphyses and periphyses, reproducing by conidia, free or in pycnidia, and by chlamydospores as well as asci. They are divided into five orders which parasitize plants and insects.

Class 3. Basidiomycetes

Fungi with well-developed mycelium which form exogenous spores, basidiospores, on basidia. A special feature of this class is the production in higher members of an elaborate fructification, e.g. toadstools, puff-balls, etc.

Class 4. Hyphomycetes (*Fungi Imperfecti*)

A large number of fungi has been provisionally grouped under this heading for want of a more determinate place for them among the representatives of the other classes. They follow an imperfect mode of reproduction culminating in the formation of conidia, transverse fragmentation of the mycelium into more or less short *arthrospores*, or in the production by a process of budding of *blastospores*. Some species, however, have already been identified as the conidial forms of higher members whose life-cycles are fully known. In other words, the *Fungi Imperfecti* could be defined as those with wholly obscure or only partially determined life-cycles.

The classification of this class is perforce wanting in conclusiveness, and the several attempts to that end are not universally accepted. Vuillemin's scheme, which separates the group on a morphological basis according to the size of the thallus and the type of spores formed, is quite practical and serves the desired purpose with a little modification. Four orders are recognized:

Order 1. *Microsiphonales* Vuillemin, 1912

Thallus of about 0·2–1μ in diameter, homogeneous, sparsely ramified, septate when young, fragmenting into bacilliform portions and forming *endospores* or *actinospores* (confined to terminal elements) which show as an efflorescence resembling powdered chalk on the colony. Saprophytes or parasites of animals and plants. This order is represented by one family, *Actinomycetaceae*.

Order 2. *Thallosporales* Vuillemin, 1910

Yeast-like fungi and yeasts that form no ascospores, reproducing by means of *thallospores*, *arthrospores* or *blastospores*, portions of the thallus adapted for reproduction, thus separating the order into two suborders:

Suborder 1. *Blastosporineae* Vuillemin, 1911

The vegetative apparatus is composed exclusively of blastospores differentiated into a pseudomycelium.

Germination is always by budding, a special feature of the group. This may take place from any part of the mother cell. The blastospores may be round, oval, pyriform, asymmetrical, stalagmoid or lacriform, bacilliform, elongated or undulating. The cells may be granular with one or more granules per cell, or vacuolated, the vacuoles containing small refractile bodies showing Brownian movement.

Fructifications develop in the form of verticils of blastospores, rudimentary, simple or compound at the nodes of the pseudomycelium, or at the end of the filaments as small chains of bacilliform or spermatozoid club-like blastospores.

Chlamydospores are a common feature in old cultures, coremia may be found in the exceptional membranous cultures, and asci occur in the ascosporous yeasts (*Hemiascomycetes*). These are the perfect forms and comprise the *Endomycetales* and *Saccharomycetales*. The imperfect forms without ascospores include (*Monilia*), *Cryptococcus*, *Atelosaccharomyces*, *Parendomyces*, and other genera.

Cultures on solid media are whitish, yellowish or bright-coloured, creamy in consistency because of accumulated blastospores, smooth, shiny, moist but not viscid, adhere to the wire loop and are easy to emulsify in water. The genus *Geotricoides* is an exception.

On liquid media floccules are formed. Filamentization can be obtained in potato water or in streak cultures on a 2% glucose-peptone-agar, or in giant cultures. Relative anaerobiosis and incubation at 37°C. are essential.

Suborder 2. *Arthrosporineae* Vuillemin, 1910

The vegetative apparatus here is a true mycelium. At first coenocytic with bi- or trifurcate ends; septa are formed later, which stage is followed finally by fragmentation at the septa. At the stage of sepatation, ramification occurs subapically.

Germination is by means of arthrospores formed by disarticulation of the mycelium, following gelification at the septa. No asci are produced. Perfect forms unknown.

Cultures on solid media are creased, dull, greyish-white, dry, viscid, velvety, and adhere to medium but not to loop. On liquid media, potato water, floccules are formed.

Both suborders have saprophytic and parasitic members.

Order 3. *Hemisporales* Vuillemin, 1910

Reproduction in this group is by means of accessory spores or *hemispores*, not enough differentiated from the thallus to merit the

term conidia. A fertile hypha bears at its tip a series of segments, *deuteroconidia*, which eventually break off and function as spores. Widespread saprophytes and parasites of man.

Order 4. *Conidiosporales* Vuillemin, 1910

True conidia are the reproductive agents in this order, which is divided into five suborders according to the various types of spores formed.

Suborder 1. *Aleuriosporineae* Vuillemin, 1911

The spores here are imperfect and are known as *aleurospores* or *aleuries*.

Suborder 2. *Sporotrichineae* Vuillemin, 1910

The spores are borne directly on the mycelium without the intervention of a sporophore.

Suborder 3. *Sporophorineae* Vuillemin, 1910

The conidia are borne on conidiophores.

Suborder 4. *Phialidineae* Vuillemin, 1910

The conidia are borne on differentiated sporophores which assume the shape of a flask and are termed *phialides*.

CHAPTER II

THE MYCOSES

Terminology. A disease provoked in man or animals through the agency of fungi is designated in a general sense as a mycosis. For further specification it may be referred to by means of an anatomical terminology which points to the site of the lesion produced in the body, and we thus talk about a "dermatomycosis," an "onychomycosis," etc., regardless of the name of the causative organism. On the other hand, a mycological terminology is sometimes employed in which the parasite is mentioned without reference to its habitat, e.g. "actinomycosis," "mucoromycosis," etc.; or else a combination of terms, such as "pulmonary aspergillosis," defines the infection. Finally, clinical names like "Madura foot," "ringworm," "pityriasis," etc., have been coined to denote certain affections which have earned that distinction as clinical entities by virtue of their frequency and consistency in attacking particular tissues and inducing definite lesions and clinical pictures.

In describing the mycoses it would obviously be best to follow one type of classification, either mycological, clinical or anatomical, but the wide variety and multiplicity of the parasites concerned and the polymorphism of the lesions they cause in the different tissues and organs of the body preclude such an ideal policy. In arranging the ensuing accounts of the mycoses of man, therefore, overlapping and some lack of uniformity have perforce been unavoidable, and the scheme is a compromise between the three classifications, with a tendency towards botanical grouping.

Reservoirs of parasitic fungi. It is now a more or less established conclusion that fungi exist in nature mostly as saprophytes, and only when accidentally introduced into man or animal do they, or at least some of them, find in their new habitats sufficient encouragement to remould their lives and assume parasitic and sometimes virulent characters. Most probably some such species as the dermatophytes, for example, have made that transformation since time immemorial and settled down for good as parasites, their ancestors meanwhile having become extinct: the saprophyte thus degenerating in a down-scale evolution into a parasite. In this way nature provides an

apparently inexhaustible reservoir of saprophytes periodically and by accident settling and becoming parasitic on man and animals; these latter, in their turn, acting as a reservoir of parasites which are passed on to man. In this respect it is significant that rural life and occupations, entailing as they do attendance on or association with animals, provide the greatest chances of fungous infections. Of the vast number of species isolated, diagnosed as old or given new names, comparatively few have been recorded a second time from the same tissue or organ, which fact bears out the hypothesis of the saprophyte changing under accidental circumstances into a facultative parasite.

Incidence and climatology. Adult males are generally more exposed and consequently most liable to infection and, with few exceptions, the incidence is highest among them. Atmospheric temperature plays an important rôle in mycoses, which are more prevalent in tropical and subtropical zones. Humidity and dryness seem to be conditions equally as effective in favouring the existence of the fungus or its spread. While moisture is really essential for the organism, dryness helps the spores to be disseminated by air.

Avenues of infection. Simple deposition on some tissues of the elements of some particular species is enough for the parasite to establish itself and extend. Apart from this, the fungus may have to be inoculated into the host by penetration of an infected foreign body, an important method of introduction, by contamination of a traumatically or pathologically denuded surface, by inhalation, or through the gastro-intestinal tract.

In spite of this knowledge, it is reasonably admissible that there must be innumerable instances where fungi, and probably virulent ones, gain access into man or animal by one or other of these ways without taking root or doing any damage. A broadly applicable rule is that healthy tissues are more likely to resist the parasite than parts already devitalized by disease or trauma.

Habitat. Practically no part of the body seems to escape mycotic infection either as the site of a primary lesion or by a secondary involvement through contiguity or by metastases. Although, except in a limited number of cases, any species may attack any tissue, there is a predilection which certain organisms exhibit for particular parts where they seem to encounter the most fertile field in which to flourish. Lastly, some species are normal inhabitants of or on the body, existing, like some yeasts, on the unbroken skin or in healthy intestines as harmless occupants.

Reaction of host to parasite. This is to a certain extent determined by the specific nature and the intensity of virulence of the fungus, and is only modified for better or for worse by the host's power of resistance at the beginning and during the course of the disease. On the whole, however, the reaction follows the lines of a chronic infection and the symptoms are the outcome of mechanical irritation and the circulation in the body of some toxic product of the parasite. Some fungi end by having the upper hand of the patient in a direct manner irrespective of the fight the body might put up, or indirectly in alliance with a pre-existing or intercurrent disease.

Occasionally, spontaneous cure, the result of some obscure phenomenon, may take place, as in the case of some ringworm fungi of the scalp which tend to disappear about the age of puberty; or else, as in favus of the hair, the parasite, by destroying the hair and stifling its follicle, brings about its own undoing.

Reaction of parasite in host. A condition for a fungus to thrive in a host is its ability to adapt itself to its environment in which body temperature is an important but not the only factor. The parasite has also to contend with the degree of receptivity and predisposition in the host comprising chemical, glandular and probably hereditary influences. The morphology of a fungus in a tissue is, as a rule, totally different from the form it takes after insemination on artificial media, and even here, the constituents of the medium influence the germination or suppression of some morphological elements. The two guises which the one organism assumes, as a saprophyte on artificial media or as a parasite in the host, can be explained as due to nutritional causes in the culture medium and as an adaptation in the presence of the phenomena of resistance which the body may launch against it. The possibility is that the tissue forms, simple of construction as they are, are best suited for an easy existence within the host and it often happens that an artificially reared parasitic species may have its virulence attenuated or even completely lost in its passage from tissue to culture, apparently by virtue of the change to a higher and more complicated organization. It can be said with little reservation that a fungus remains more or less localized where it happens to be implanted, doing limited damage and increasing in none too prolific a manner. Most of the serious harm in a few infections is due to metastatic fragments breaking off and reaching fresh sites in cases which have a tendency to become generalized, the host having, as a result, to contend with multiple infections, some of which might be in vital organs.

CHAPTER III

MYCETOMA

Maduromycosis and Actinomycosis

Definition. A chronic inflammatory granulomatous hypertrophic tumour brought about through infection with certain fungi, destroying and deforming principally the foot, though practically any part of the body may be involved. It contains grains of variable size, shape and colour, formed partly of matted mycelium with the addition, in some types, of club-like bodies, apparently swellings of hyphal tips. In time the pathological products are discharged suspended in pus through multiple sinuses and fistulae. Two forms are recognized, *Maduromycosis* and *Actinomycosis*.

Maduromycosis or "Madura Foot"

Historical. This condition was first reported from Madura in 1842 by Gill as a fungoid tumour of the foot and later, also from Madura, by Colebrook (1846) as *Madura foot*, a name already employed for a similar infection in the south of India, where cases were described by Heyne as far back as 1806. The term *Mycetoma* for the same disease was used in 1860 by Carter, who studied it in detail and subsequently determined its fungous origin. Further investigations by other workers have brought our knowledge of the subject to its present pitch and incriminated several species as responsible for the infection.

Definition. Maduromycosis is characterized by the formation of grains composed of septate large-sized hyphae, usually over 1μ in diameter, with definite walls, often producing chlamydospores, and is due to infection with a variety of species excluding those of the genus *Actinomyces*.

Aetiology. The grains in the tumours vary in colour with the different aetiological agents, and may be black, white, yellowish or red, as shown in the following table. In the black variety, species of the genus *Madurella* are more often than not the offending organisms. Species of *Indiella* are usually isolated from the lighter grained maduromycotic mycetomas although, on the whole, light grains are to be found in actinomycosis.

Species producing Black Grains

HYPHOMYCETES

Trichosporium khartoumensis (Chalmers and Archibald, 1916) Dodge, 1935; Sudan; foot.

T. clapieri (Catanei, 1927) Dodge, 1935; Africa; maxillary region.

Monosporium apiospermum var. *peperei* Sartory, 1922; Sardinia; pathogenic to laboratory animals.

Madurella mycetomi (Laveran, 1902) Brumpt, 1905; Carter's black mycetoma; cosmopolitan; commonest cause of mycetoma; rough, fragile, black or reddish-brown grains; non-pathogenic to guinea-pig.

M. bouffardi (Brumpt, 1906) Dodge, 1935; Bouffard's black mycetoma; Somaliland; foot; black, smooth, slightly elastic grains which unroll when placed in water into filiform structures; experimental inoculation negative.

M. tozeuri (Nicolle and Pinoy, 1908) Pinoy, 1912; Nicolle and Pinoy's black mycetoma; Tunis; skin of foot only involved in spite of eighteen years' duration.

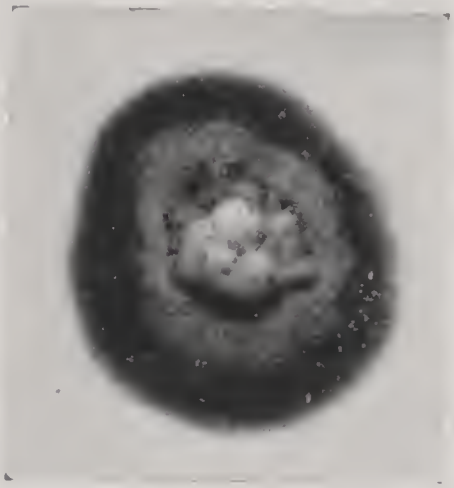


FIG. 9. *Torula jeanselmei*. Colony on 2 per cent Sabouraud glucose-agar. Case of black grain mycetoma. (Original)

M. bovoi Brumpt, 1910; Bovo's black mycetoma; Italy; mycetoma of the foot with grains in the groin.

M. tabarkae Blanc and Brun, 1919; Tunis; subcutaneous; followed upon a street accident to the foot.

M. ramiroi P. da Silva, 1919; Bahia, Brazil; foot; non-pathogenic experimentally.

M. oswaldoi P. Horta, 1919; Brazil.

M. americana Gammel *et al.*, 1926; Cleveland, Ohio; the first American case of black-grained mycetoma of the foot; non-pathogenic to laboratory animals.

M. ikedae Gammel, 1927; Minneapolis; non-pathogenic to rabbit or guinea-pig.

Torula jeanselmei Langeron, 1928; Antilles, Egypt; foot; grains formed of mycelial elements rolled upon themselves.

ASPERGILLACEAE

Penicillium mycetomagenum Mantelli and Negri, 1915; Italy; foot; ? contaminant in a *Madurella mycetomi* infection (Vuillemin, 1931).

? *Aspergillus mycetomi* Villabruzzi and Gelonesi, 1927; Italian Somaliland.

MUCORACEAE

Mucor mycetomi Gelonesi, 1927; Italian Somaliland.

Species producing White or Yellowish-White Grains

HYPHOMYCETES

Indiella mansoni Brumpt, 1906; Brumpt's white mycetoma; India, China.

I. reynieri Brumpt, 1906; Reynier's white mycetoma; Paris, Greece; the first case of a maduromycotic mycetoma occurring in France; grains of a complex vermiform appearance.

I. brumpti P. da Silva, 1922; Brazil.
Monosporium apiospermum Saccardo, 1911 (=*Indiella americana* Delamare and Gatti, 1929); Tarozzi-Radaelli white mycetoma; North America, Brazil, Paraguay, Europe; cutaneous involvement of foot.

ASPERGILLACEAE

Aspergillus nidulans var. *nicollei* Pinoy, 1906; Nicolle's white mycetoma; Tunis; foot; non-pathogenic to rabbits or guinea-pigs.
Allescheria boydii Shear, 1921; Texas, Egypt; foot; inoculation presumably from a thorn.

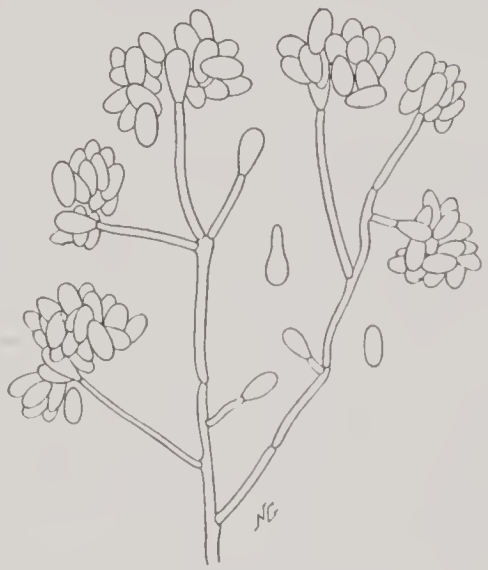


FIG. 10. *Allescheria boydii*. Cultural morphology. Case of white grain mycetoma. (Original)

Species producing Greenish-Yellow Grains

ASPERGILLACEAE

Aspergillus amstelodami (Mangin, 1909) Thom and Church, 1926; Brazil; foot.

Species producing Red Grains

HYPHOMYCETES

Rubromadurella langeroni Talice, 1935; Uruguay.
Glenospora semoni Chalmers and Archibald, 1917; Carter first described a case from India and Semon cultivated the organism from the foot of an Indian in the British Army in France.

ASPERGILLACEAE

Aspergillus sp., Balfour and Archibald case; Africa.

Geographical distribution. The infection is most prevalent in the tropical, subtropical and temperate zones of Asia, Africa, Europe and America. In the Sudan, it is interesting to note, the disease is recognized by the natives under the Arabic name "Nabt Hindi Nabet," which when literally translated means "sprouting Indian

growth," a description either suggesting the close similarity between the Sudanese and Indian mycetomas or referring to India as the source of introduction.

Morbid anatomy. This varies only to a slight extent with the site of infection and the causative organism. The body reacts poorly against the presence of the parasite and there first occurs a lymphocytic infiltration around the fungus followed by the formation of uni- or multinucleate epithelioid cells, giant cells and fibrous tissue, the latter entangling the fungus and the vessels in the vicinity with accompanying peri- and endarteritis. This institutes the formation of the grain.

On section, a grain proves to be composed microscopically of a central more or less homogeneous area with some haemorrhage from ruptured capillaries, and in this matrix the actual grain with its component mycelial elements is embedded. Surrounding this zone is a layer of inflammatory tissue of lymphocytes, polymorphonuclear leucocytes, epithelioid cells and giant cells, the lot being enclosed in fibrous and connective tissue.

As destruction and degeneration of the part proceeds, sinuses and fistulae as well as intercommunicating cavities are produced, and the pathological contents of the tumour are discharged in the form of an offensive oily, purulent, occasionally blood-stained exudate in which are suspended the characteristic grains. These may be small or large, from microscopic dimensions to 1 mm. or a little more in diameter, single or aggregated in a mass sometimes the size of a pea. In consistency, they are soft, elastic or hard, smooth or coarse, and assume various hues due to pigmentation by the secretions of the responsible species in each case.

The infection spreads by continuity or through the lymphatics or blood-stream, and metastatic foci may be started in different remote situations. In some cases, the glands draining an infected area may become enlarged, partly as a result of secondary infection. The soft and semi-soft tissues, cartilages and tendons are often involved; but contrary to what happens in actinomycosis the bones are usually spared. On section, the mycetoma presents a greasy surface, with channels and cavities, the destructive process leaving the normal anatomical structures hardly recognizable.

Symptoms. The lesion generally begins on an exposed part of the body, the sole of the foot in bare-footed individuals, the hand, knee, or practically anywhere where the fungus has penetrated through a scratch or after a prick from a thorn or splinter of wood presumably

carrying the organism as a saprophyte. The trauma may pass unnoticed until, after a latent period of very variable length, weeks, months or even years, the initial sign appears in the form of a painless, firm, slightly discoloured, well-defined hemispherical nodule, about half an inch in diameter, which breaks down into an abscess in a few weeks' time and discharges the characteristic pus and grains. The condition spreads gradually by repetition of this process; the formation of fresh nodules extending over years, in the course of which the tumour grows gradually in size and causes deformation of the

FIG. 11. "Madura foot." Case of white grain mycetoma. (Original)

affected part which becomes riddled with multiple discharging sinuses and fistulae.

Metastatic deposits may occur and produce signs and symptoms referable to the particular tissue or organ involved. Pain is generally absent, and fever, an inconstant feature, is low if at all present. The main inconvenience to the patient is the bulk of the mycetoma, which interferes with the movements of the infected limb, hinders locomotion and leads to disuse atrophy of the muscles proximal to the tumour. The disease is never as generalized as actinomycosis, and, untreated, it goes on for years, with an exceptional possibility of spontaneous cure.

Diagnosis. The discovery of the grains in the pus, and the cultures, if made, clinch the diagnosis. Weak scabs usually form over the

sinuses, but are easily removed and, with a little squeeze, the grains can be expressed mixed with blood and pus. Clinically, maduromycosis has to be differentiated from actinomycosis, sporotrichosis, tumours of tuberculous or syphilitic natures, framboesia, angiokeratoma, filarial swelling, etc.

Treatment. Iodides, unfortunately, are not as effective here as in actinomycosis, but should be administered nevertheless in large doses in conjunction with novarsenobenzol, or with mercurochrome alternately with novarsenobenzol intravenously. Sulpha preparations are sometimes effective. Combined medical and surgical measures are often necessary.

Actinomycosis and Actinomycotic Mycetoma

Historical. Lebert (1848) was the first to discover actinomycosis in man although it was known in cattle from a very early period. In 1877 Bollinger and Harz determined the mycotic nature of the osseous affection clinically termed "Lumpy Jaw" in cattle, and Harz named the fungus *Actinomyces bovis*, but did not cultivate it. Since then, Boström (1885) considered a culture obtained by him aerobically, which he also named *A. bovis*, as the aetiologic agent of cattle actinomycosis. More species continued to be isolated from cattle infections and labelled with the same or given new names, such as *A. sulphureus* Gasperini, 1894, etc. In 1891, Wolff and Israel grew from two human cases of actinomycosis, retromaxillary and pulmonary infections, an anaerobic strain which Kruse (1896) called *Streptothrix israeli*. This is claimed to be the true cause of the classical actinomycosis in man and cattle, while the original *A. bovis* Harz, 1877, remains an indeterminate entity, as no culture of it was made, while Boström's species might have been a saprophytic contaminant. But, as the name *A. bovis* has the priority, it is still retained and regarded by some as the parasite in cattle, while by others

FIG. 12. *Actinomyces bovis*. Colony on 2 per cent Sabouraud glucose-agar.

the anaerobic species *Actinomyces israeli* (Kruse, 1896) Dodge, 1935, is recognized, and rightly so, as the agent in both human and cattle

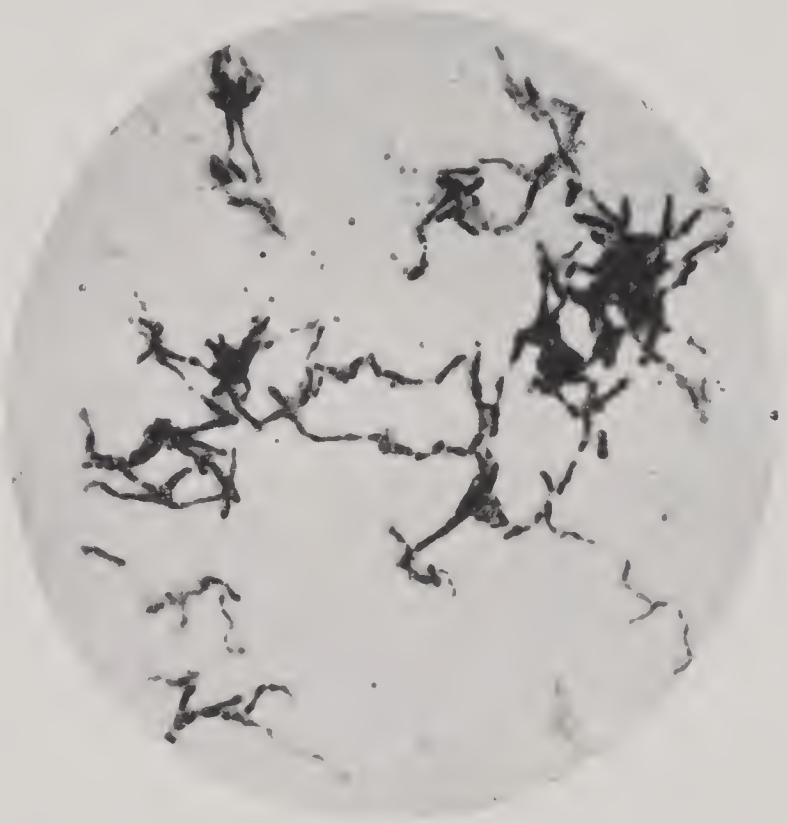


FIG. 13. *Actinomyces israeli*. Smear from culture showing bacillary and coccoid forms stained in streaks and spots. (Original)

actinomycosis. It is notable that organisms similar to Boström's species are common in soil and decaying vegetable matter. Israel's species, on the other hand, while commonly present in decayed teeth, tartar deposits and tonsillar crypts, has so far not been isolated as a saprophyte in nature in the same way as *A. bovis*.

Apart from the histories of the parasites in cattle and in man and the confusion that has arisen so far concerning the nomenclature of the organisms having affinities with *Actinomyces*, several species have been implicated in human infections and will be mentioned under aetiology as they were reported at different times from various lesions all over the world. Most of them, for

FIG. 14. *Actinomyces asteroides*. Colony on Sabouraud 2 per cent glucose-agar. Case of white grain mycetoma. (Original)

want of better classification were transferred provisionally, if not permanently, for the sake of convenience into the genus *Actinomyces*.

Definition. Actinomycosis and actinomycotic mycetoma are characterized by the formation in the lesions of grains composed of non-septate mycelium, about 1μ or less in diameter, with ill-defined walls and producing no chlamydospores, as well as by club-like bodies which may, in some instances, be additional constituents of the grains. The term "actinomycosis" is regarded as a general designation for the infection, which may or may not culminate in the production of an external tumour or mycetoma.

Aetiology and geographical distribution. The aetiology is restricted to members of the genus *Actinomyces*. As in maduromycosis, the grains in the lesions may be of different colours and are accompanied or otherwise by clubs according to the pathogenic species tabulated below:

Actinomycosis with Black Grains

These have been recorded by the following authors in cases from which no cultures were made:

Babes (1888) and Mironescu (1910), from Roumania; F. de Almeida (1930), liver, from Brazil; and Beron (1931), from Bulgaria.

Actinomycosis with Yellow or Yellowish-White Grains

With clubs:

Breviora

Actinomyces israeli (Kruse, 1896) Dodge, 1935; cosmopolitan; bones mainly affected.

A. thibiergei (Ravaut and Pinoy, 1909) Greco, 1916; subcutaneous and intramuscular nodules.

Majora

A. mexicanus Boyd and Crutchfield, 1921; foot; North America; non-pathogenic for guinea-pigs.

A. transvalensis (Pijper and Pullinger, 1927) Nannizzi, 1934; foot; South Africa; pathogenic to guinea-pig.

A. pretorianus (Pijper and Pullinger, 1927) Nannizzi, 1934; axillary region and shoulder; South Africa; pathogenic to guinea-pigs.

Without clubs:

Breviora

A. krausei (Chester, 1901) Brumpt, 1927; abscess of lower jaw; Germany; ? synonym of:

A. ponceti (Verdun, 1912) Brumpt, 1927; ? pseudo-actinomycosis; Europe.

Minora

A. asteroides (Eppinger, 1890) Gasperini, 1894; Musgrave and Clegg's white mycetoma; cosmopolitan; peritonitis, meningitis; pathogenic to laboratory animals and monkeys.

A. freeri (Musgrave and Clegg, 1907) Bergey, 1923; pathogenic to experimental animals; ? synonymous with *A. asteroides*.

A. madurae (Vincent, 1894) Lachner-Sandoval, 1898; Vincent's white mycetoma; bones hardly affected; foot; cosmopolitan; non-pathogenic to experimental animals.

A. brasiliensis (Lindenberg, 1909) Gomes, 1923; Lindenberg's white mycetoma; thigh and leg; Brazil; non-pathogenic to laboratory animals.

A. convolutus (Chalmers and Christopherson, 1916) Brumpt, 1927; Sudan; non-pathogenic to monkeys or laboratory animals.

A. bahiensis (P. da Silva, 1919) Brumpt, 1927; Brazil.

A. serratus (Sartory *et al.*, 1930) Dodge, 1935; bone; pathogenic to guinea-pig and dog.

A. brumpti Bordjoški and Milochevitch, 1935; foot; Yugoslavia.

Majora

A. liquefaciens (Hesse, 1892) Brumpt, 1927; inguinal region; Europe; non-pathogenic to laboratory animals.

A. garteni (Brumpt, 1910) Brumpt, 1927; abscesses; Europe; pathogenic to guinea-pig, rabbit and pigeon.

A. nicollei (Delanoë, 1928) Nannizzi, 1934; thigh, starting in the inguinal glands; Morocco; pathogenicity negative after four years' subculturing.

Actinomycosis with Red or Reddish Grains

Without clubs :

Breviora

A. pelletieri (Laveran, 1906) Brumpt, 1927; Pelletier's red mycetoma; Egypt, Senegal, India; attacks various parts of the body.

A. africanus (Pijper and Pullinger, 1927) Nannizzi, 1934; foot; bones affected; grains carmine red; pathogenic to guinea-pig.

A. genesii (Fróes, 1930) Dodge, 1935; grains extremely hard and abundant; foot; Bahia, Brazil.

Minora

A. somaliensis (Brumpt, 1906) Brumpt, 1927; Bouffard's white mycetoma; causes complete destruction of bones; grains hard, practically insoluble, parasite seems to secrete a resistant crust around it; Somaliland, Sudan and Central Africa.

The records by various authors show that actinomycosis is a cosmopolitan infection, present in the two hemispheres and occurring more frequently in rural areas where cattle are bred in large numbers.

Morbid anatomy. This is, on the whole, similar to the pathological changes which take place in maduromycosis. In addition, the bones are generally affected, the destructiveness is more pronounced and the tissue reaction greater, with more extensive formation of connective tissue. Metastatic involvement is also more common and is effected via the venous circulation in the majority of cases. In most instances the primary lesion occurs in the skull, and metastases may be carried to the brain or along the prevertebral space to the mediastinum.

Primary infections of the gastro-intestinal tract come next in the order of frequency, the fungus being introduced through the mouth. The oesophagus is then the seat of the initial lesion, and by continuity, the mediastinum, lungs and heart may become involved. In the abdomen, the stomach and intestines, especially the caecum or appendix, are the sites of election, and ulcers are produced from which, by adhesions and suppuration, the spleen, liver, kidneys or bladder may be infected. Involvement of the peritoneum is likely to lead to peritoneal abscesses and spread to the abdominal wall along the psoas muscle to the hip or, by way of the retroperitoneal space, the morbid process may ascend up to the thorax or extend down to the ischio-rectal fossa and perineum with resulting abscesses and sinuses. Primary pulmonary infection is fairly frequent and begins in the bronchi in the form of a superficial catarrh followed by a destructive inflammation with the formation of granulation tissue and abscess cavities, the whole process closely resembling pulmonary tuberculosis. Extension from the lungs to the mediastinum occasionally leads to pleurisy and often to abscesses and sinuses in the thoracic wall. The right lung is more commonly affected than the left and the apex or base may equally be the site of the lesion. Infection of bones leads to the separation of sequestra which may be discharged together with the grains from the sinuses and fistulae.

Microscopically, besides the grains with their soft central area, the surrounding lymphocytic infiltration, epithelioid cells, giant cells and fibrous tissue present in maduromycosis, some actinomycotic lesions include certain bodies (clubs) of a problematical origin and function which require special consideration.

Clubs in Actinomycosis

The hyphae in some species of *Actinomyces*, either in the infected tissues, in culture, or in both, present swellings at their extremities as club-like microscopical bodies of various shapes and sizes.

Far from being a peculiarity of some species of that genus, they have been found in a variety of states, pathological and otherwise, where mycelium is absent. By their nature, these conditions leave the exact function and true origin of these bodies rather uncertain. They probably represent the outcome of a process in which both the host's tissue elements and the fungus have a share. To consider the parasite as wholly responsible for their production might apply in some cases, but certainly not in others. Clubs have been known to form around

dead tubercle bacilli, organic substances and even inorganic matter that could hardly play a part in their production. They are reported to have occurred in some staphylococcal infection, in the presence of several acid-fast organisms, with *Bacillus leprae*, in maduromycosis caused by *Monosporium apiospermum*, in sporotrichosis and in the course of some experimental blastomycosis and tuberculosis. One of the theories expounded is that their appearance is a symbiotic phenomenon between the parasite and the host.

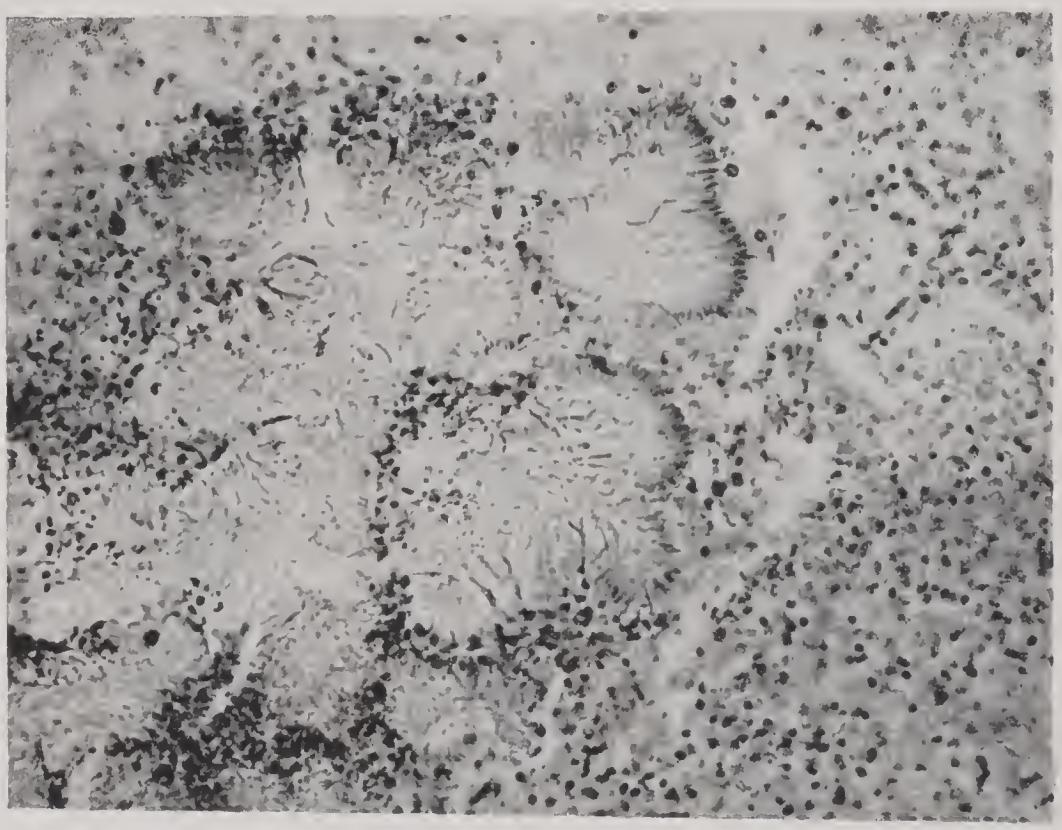


FIG. 15. Section of an actinomycotic grain with clubs darkly stained peripherally. (Original)

On the whole they are most probably formed through an interaction between host and parasite, a club being a terminal chlamydospore, a concentration of protoplasm, or simply a blind end of a mycelial filament assuming that blunted shape as it comes up against a barrier of reactionary epithelioid cells, giant cells and fibrous tissue which check its further progress into fresh territory; in fact, in some instances in old grains, it actually ends by degenerating and is transformed into calcarious deposits.

Symptoms and course. The means by which the fungus is introduced into the body are similar to those in maduromycosis, by

subcutaneous inoculation on a penetrating foreign body and, in addition, by ingestion or inhalation in internal actinomycosis. From carious teeth, tonsillar crypts and from the apparently normal mouth, mycelium and granules of *Actinomyces* have been recovered and strains of *Actinomyces* and *Actinomyces*-like organisms have been grown. These situations may act as permanent reservoirs from which infection may attain devitalized, bacterially invaded or in some way predisposed or sensitized parts of the body. A predisposing allergic sensitization of the host is a theory which has its supporters. Rural occupations increase the chances of infection; farm labourers in contact with soil and cattle being more frequently affected. The prevalence is greatest among males, while young children usually escape, the varying degree of incidence being merely a question of exposure.

FIG. 16. Actinomycotic mycetoma due to infection with *A. asteroides*. (Original)

The onset of the disease is insidious and the course very chronic. The symptoms vary with the morbid changes in the different tissues and organs affected. It would, therefore, be superfluous to enumerate all the possibilities in clinical signs and symptoms which can easily be guessed at from a consideration of the pathological anatomy of the disease in the various parts of the body.

Cervico-facial cases are commonest, show no tendency to generalization and are amenable to treatment. Thoracic and then abdominal infections come next in order of frequency. Lesions in other situations are rare; meningitis, endocarditis and infection of the ovary are reported and generalization through the blood stream is occasionally seen.

Pyrexia and pain are inconstant symptoms, and it is uncommon for the disease to take the form of an acute inflammatory process with high fever although it has been known to happen. Intercurrent disease, wasting and cachexia are the final stages before a fatal termination. The prognosis depends largely upon the site of the lesions, but is generally grave where these are extensive or deeply

seated. Spontaneous cure is very exceptional and recurrence is possible after apparent healing.

Differential diagnosis. Actinomycosis may attack any organ or tissue, and the symptoms and signs are liable to be mistaken for many other affections of the part concerned. The lesions, whether primary, by extension or by metastases, often give true pictures of more common diseases. Infections in the chest, for example, closely simulate pulmonary tuberculosis, pneumonia, pleurisy, or even simple bronchitis, especially in the earlier stages, endocarditis or mediastinal tumours. If situated in the abdominal cavity a host of conditions, among which are gastric or duodenal ulcers, colitis, appendicitis, peritonitis, etc., will have to be excluded. Infections on the face, commonly met with, may be mistaken for abscesses or sinuses due to dental caries. When the lesion is cutaneous, it has to be distinguished from syphilides, lupus or simple abscesses, and from pleurisy with sinus formation if situated on the chest wall. Appearances in radiographic pictures where bones are involved may be erroneously diagnosed as a tuberculous process or as a pyogenic osteomyelitis. The possibility of neoplasm should also be borne in mind; in fact, this disease requires a wide clinical survey for its diagnosis, apart, needless to say, from mycological findings. Finally, mycetomas of actinomycotic aetiology will naturally have to be distinguished from maduromycosis, the distinction resting on culture results.

Diagnosis. The pathological material is examined fresh for grains and mycelium, with the naked eye and under the microscope in a 30% warm or cold solution of potassium hydroxide. The grains may have to be expressed through sinuses by pressure on the neighbouring parts. For microscopic examination they are lightly crushed between slide and cover-slip, and the presence or absence of clubs is ascertained. If the grains are too small and scanty, the pus can be washed and centrifuged once or twice in the potassium hydroxide solution. Cultures from grains or material removed from deep down in the lesion under aseptic conditions will often lead to the determination of the infecting species. Tissues excised by operation may be cut into sections, stained and examined as an aid to more accurate diagnosis.

Treatment. Potassium iodide in heavy doses, 10 grammes daily, has often given good results, especially in early cases. Iodine preparations intramuscularly or intravenously and X-ray therapy have also proved useful. Sulphanilamide and allied drugs as well as prolonged penicillin administration and vaccines may be tried. In

most cases, however, surgical measures and perhaps amputation may become imperative, but this radical procedure should only be resorted to as a last attempt to save the patient's life.

Actinomyces israeli in the lesions: Granules serpigenous, composed of more or less elongated Gram + ramified filaments or coccoid forms; Gram − acidophile clubs.

In culture: *Breviora* type of culture, yellowish, short filaments, swollen at one end (*Corynebacterium* type), staining in streaks or spots, clubs rare. Microacrophile and carboacidophile facultative anaerobe. Colonies resemble dew-drops on serum-agar.

Actinomycetaceae-Mycological Study

The pathological material, whether or not containing mycelium or grains, is obtained from deep down in the lesion under aseptic conditions. A 2% glucose medium glycerinated to the extent of 5% suits most purposes for aerobic species. Anaerobic species which are usually the aetiological agents in human and bovine actinomycosis are grown on inspissated serum at 37°C. If grains are obtainable, they are crushed between two sterile large slides, which are then separated and the material transferred into four tubes of coagulated Loeffler's glucose-serum. Two of these tubes are put uncovered in an atmosphere of CO_2. The other two are sealed with paraffin and the lot incubated at 37°C. Growth may be expected at the end of three days.

When cultures are obtained, the first step in their recognition is arrived at by identifying them with one of three groups, each with its special characters as follows:

Majora	*Minora*	*Breviora*
Aerobic	Aerobic	Anaerobic for preference
Free growth and spread at 22°–37°C	Moderate growth and spread at 22°–37°C	Difficult to grow
Cultures with chalky bright efflorescence	Cultures tarnished, powdery appearance with age	Neither efflorescence nor powdery appearance
Hyphae coarse, ramified	Fine hyphae, rarely branched	Hyphae as bacilliform elements
Earthy or mouldy odour	Odourless or faintly mouldy	Odourless, sometimes faeculent
Gram +	Gram +	Gram +
Acid-fast	More or less acid-fast	More or less acid-fast
Liquefy gelatin (proteolytic), digest well-cooked starch (amylolytic), coagulate serum	Proteolytic action rarely present, amylolytic action usually absent	Proteolytic and amylolytic actions absent
Grow on potato	Poor growth on potato	No growth on potato

Species of *Actinomyces* may be stained with Gram, in which case the myeelium, which is basophilic, appears as Gram+ ramified filaments, diphtheroid bodies and eoecoid forms. If the smear is further treated with 1% acid Fuehsin, the elubs when present, being acidophile, will be Gram—. The intense red background and the clubs ean be differentiated with plain water until the required point is reached. This is best performed under the microscope, and further deeolourizing can be arrested by means of water slightly aeidulated with acetie aeid.

Actinobacillosis

Actinobacillus lignièresi Brumpt, 1910, an aerobic species which has marked affinities with the genus *Actinomyces*, causes the actinobacillosis of cattle as described by Lignières and Spitz. This infection is only distinguishable from actinomycosis in so far as it respects bones and generally affects the soft parts in the head and neck and in the abdominal cavity.

In 1909 Ravaut and Pinoy reported the organism from an Argentine suffering from otitis, which was followed, after apparent cure by operation, by meningitis. In another case with a fatal termination reported by Beaver and Thompson in 1933, the lesions found postmortem were in the nature of granulomatous abseesses in the lungs, liver and spleen.

Cultures of this organism, whose exact systematic position is still rather undetermined, lack the myeelial element and assume bacillary, streptobacillary or coecoid forms. Langeron *et al.* (1925) obtained elubs in cultures from two eases of bovine actinobacillosis, and they maintain that the disease is caused by more than one type of parasite. In smears from culture the organism appears as Gram— rods.

Nodosités Juxta-Articulaires

This refers to a ehronie condition occurring in natives of tropical and subtropieal eountries, and takes the form of subcutaneous periartieular nodules over the bony prominences of the body which usually eome in contact with the ground while the native sleeps or squats.

Cases have been recorded relating to white patients who have never been out of Europe, where the disease is uncommon, as well as to others who have lived for some time in endemic areas where they probably contraeted the infection.

Described first by Macgregor in 1901 in New Guinea, these nodules were further investigated by Steiner in Java and in Siam by Jeanselme, to whom we owe the French name. Fontoynont and Carougeau in Madagascar found in these swellings grain-like systems with mycelial filaments, giant cells and peripheral fibrous tissue, which findings were confirmed later by other workers elsewhere; but the fungus, *Actinomyces carougeaui* (Gougerot, 1909) Brumpt, 1929, was never cultivated. The occurrence of similar nodules in syphilis and yaws has led to the supposition of a treponemal aetiology even in cases with negative Wassermann reaction, and *Treponema pallidum* has actually been isolated from the nodules. In Brumpt's opinion, the organism is in the nature of a pseudo-parasite composed of amyloid elements.

Symptoms. Either introduced through slight skin traumata or otherwise, the parasite at first produces very small, soft and discrete movable subcutaneous nodules, which fuse in time into fairly large hard tumours adherent to the overlying skin, which is generally unaltered except for some stretching and perhaps ulceration from local traumatism. Knees, ankles, wrists and elbows are the sites of election, and the underlying bones are not involved. The symptoms do not amount to more than the inconvenience due to the size and situation of the swellings. Spontaneous disappearance of the tumours has been known to occur.

Diagnosis. The chronicity, consistency and situation of the nodules, together with the unchanged condition of the overlying skin, help in the diagnosis.

Treatment. Potassium iodide may be tried. Excision may have to be considered where the nodules cause great inconvenience and in chronic cases which prove refractive to iodine medication. In some instances, probably truly syphilitic, the nodules have reacted favourably to specific treatment.

CHAPTER IV

BLASTOMYCOSIS

The Blastomycoses

The blastomycoses are diseases due to infection with true yeasts, members of the subclass *Hemiascomycetes*, perfect forms producing ascospores, or with yeast-like fungi whose perfect forms are unknown, part of the *Hyphomycetes* in the order *Thallosporales*. These include the suborders *Blastosporineae*, reproducing by burgeoning and forming a pseudomycelium, and the *Arthrosporineae*, multiplying by a process of fragmentation of a mycelium into arthrospores.

Introduction into the host is generally effected through skin traumata, by way of mucous surfaces, by ingestion or by inhalation, a breach of surface, devitalization of tissue or concomitant bacterial infection in each case being apparently an essential condition. The commonest lesions are primarily of a cutaneous character and are manifested as miliary abscesses, subcutaneous nodules, tumours or gumma-like swellings, breaking down in the course of the disease into sinuses, fistulae or ulcers, and occasionally forming warty excrescences, the infection sometimes extending to the viscera in a generalized form via the lymphatics or blood-stream.

Most of the cases referred to as blastomycoses have been reported and investigated in the United States, but their geographical distribution is almost universal.

Three types of infection and evolution are recognized, but there exist no hard and fast distinctions to separate them, as more often than not the one merges into the second and may end as an example of the third.

1. The localized form in the skin or its appendages, subcutaneous tissue or mucous membrane, including lungs, intestines or serous cavities. Except for a few instances, it may run into:

2. The generalized type involving deep-seated structures and internal organs and, in some cases, leading to:

3. The systemic or septicaemic variety.

The clinical pictures and morbid changes are fundamentally alike with some variations in site, extent of damage sustained and the ultimate

result of recovery or death according to the invading species and the treatment.

Coccidioidosis
Granuloma Coccidioides
" Posadas' Mycosis "

Definition. A chronic mycotic infection, insidious in onset, characterized by nodular lesions, principally pulmonary or cutaneous, later becoming generalized and often ending fatally.

Historical. The parasite was discovered in 1892 by Wernicke in a Brazilian soldier in Buenos Aires with primary cutaneous lesions. Wernicke's pupil Posadas made an exhaustive study of it and ascertained its pathogenicity by experimental evidence.

Aetiology and geographical distribution. The organism, *Coccidioides immitis* Stiles, 1896, is the cause of this mainly American infection. Apart from the first recorded case, the disease is to a certain extent peculiarly restricted to California, where it is almost endemic, Argentina and Uruguay, but there is no reason to deny a strong probability of its unsuspected occurrence undiagnosed elsewhere. Egyptian cases have been ascertained. The species isolated from North and South America appear by their affinities to represent two strains of the same organism. Instances of the parasite being present in cattle, sheep and pigs have been reported from North America, and pulmonary infection is known among wild rodents in Arizona.

Morbid anatomy. Nodules, the main feature, preponderate in the lungs and subcutaneous tissue which are often the sites of the primary lesions. Softening and pus formation in them are late sequels when the internal organs, liver, spleen, kidneys and suprarenals, meninges and spinal cord, bones and joints become involved. The lymphatic glands are rarely affected and the intestines are always immune.

Sections of the nodules show a composition of fibrous tissue, giant cells enclosing the parasite, and lymphocytes and plasma cells in varying amounts. In the tissues, pus or sputum, the fungus occurs as spherical double-walled bodies 5–50μ in diameter, sometimes vacuolated or containing daughter cells, each surrounded by a capsule similar to that of the parent, and occasionally the walls are beset with fine needle-like projections. The organism develops into asci with numerous ellipsoid ascospores which are disseminated by rupture of the enclosing capsule. Mycelium is rarely found in the tissues, while

the opposite, rare asci and abundant mycelium, is the rule in cultures. Generalization of the infection takes place via the lymphatics and blood-stream.

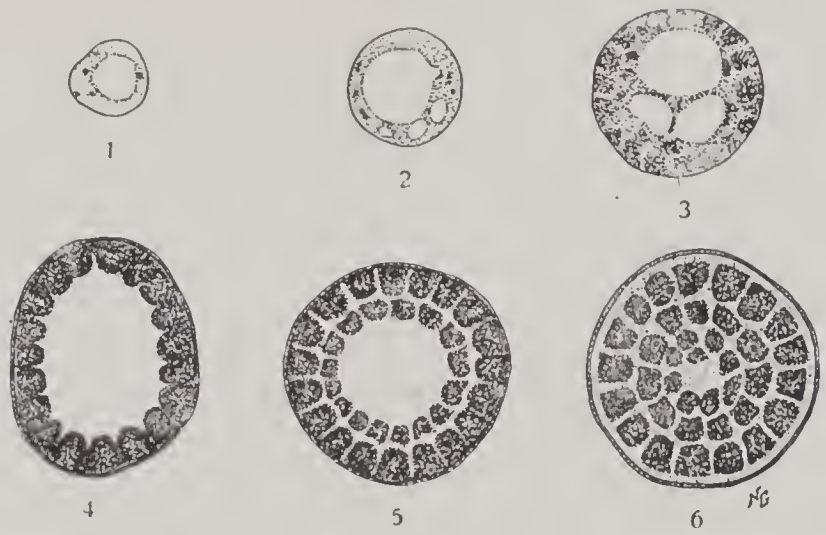


FIG. 17. *Coccidioides immitis.* Development of asci in tissues. In spore formation the ascospore nuclei migrate to the peripheral layer of the protoplasm and are separated by radial cleavage planes followed by periclinal planes until two or three layers of protospores are formed. The protospores then form groups of 2–16 spores which finally expand and fill up the whole central vacuole as they increase in size. (After Fonseca)

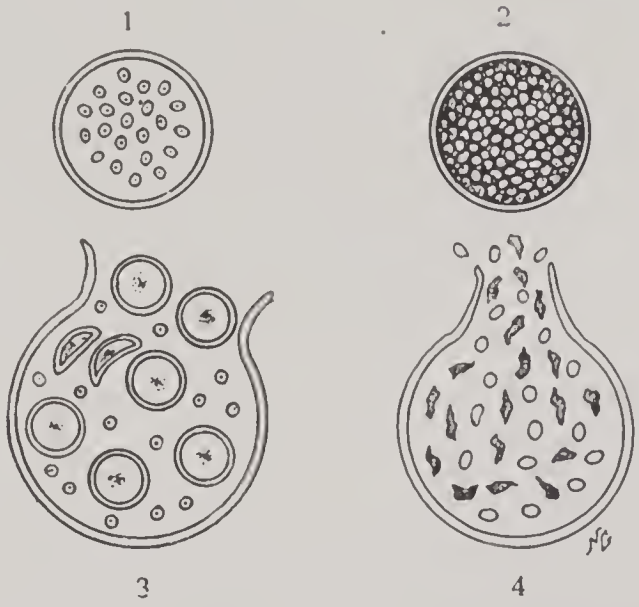


FIG. 18. *Coccidioides immitis.* Evolution. 1. young vegetative cyst, 2. young infective cyst, 3. vegetative cyst discharging young cysts, 4. ripe cyst discharging infective granular and hyaline corpuscles. (After Fonseca)

Symptoms. The avenues of introduction are the respiratory tract and through negligible traumata of the skin by thorns or other foreign bodies carrying the fungus which probably grows saprophytically on soil and vegetable matter.

The clinical picture has no uniformity. After a long incubation period and vague constitutional disturbances of general malaise and irregular pyrexia, the primary lesions, which are usually cutaneous or pulmonary, begin to form and later induce secondary generalization. Pulmonary symptoms followed by secondary cutaneous involvement may show first, and occasionally articular, osseous, meningeal, spinal or pelvic manifestations are the starting points of the disease. There is a case on record where the scalp was first affected, and in some instances the mucous membrane of the mouth or nose is the

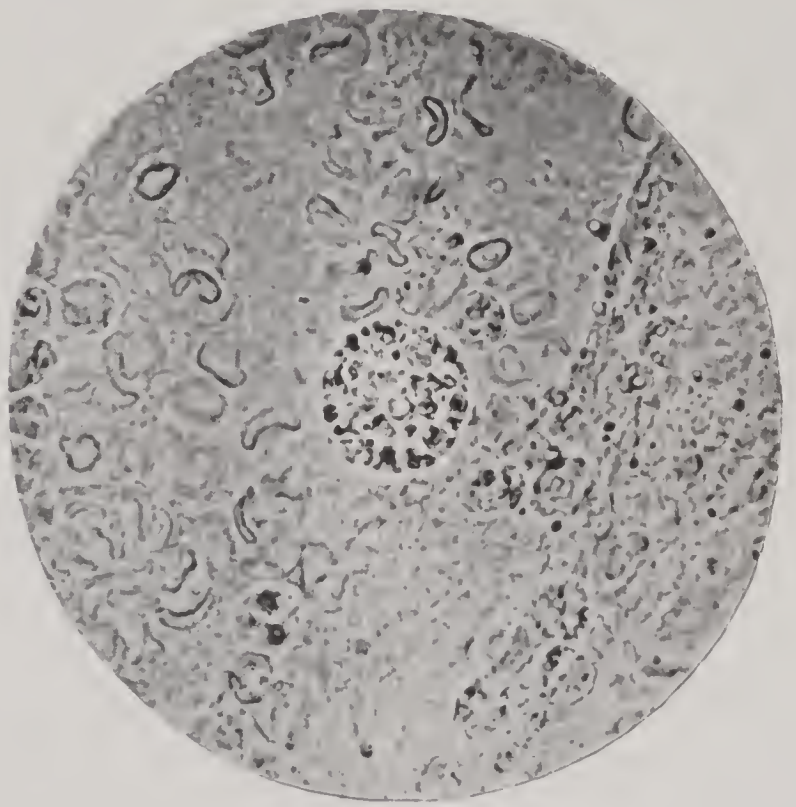


FIG. 19. *Coccidioides immitis.* Ascus in purulent discharge from a sinus in the foot. (Original)

focus of the initial lesion. Other alternatives of primary and secondary localizations have also been reported. A case presenting the clinical picture of Madura foot in which the asci were discovered first in the discharge from the sinuses is recorded from Egypt.

The skin manifestations are generally in the form of subcutaneous painless, discrete or confluent nodules, and may be accompanied by papular or pustular eruptions. Miliary abscesses, or joint and bone lesions suggestive of osteomyelitis, have occurred in cases of primary infections of the lungs. The cutaneous and pulmonary signs are liable to be mistaken for those of tuberculosis. Leishmaniasis,

neoplasms and mycosis fungoides of the skin are among the wrong diagnoses. Metastases are carried along the blood-stream or lymphatics and, in the rare cases in which glandular enlargement takes

FIG. 20. Coccidioidal granuloma of the knee. (Original)

FIG. 21. *Coccidioides immitis* cutaneous lesions. (By courtesy of N. F. Conant)

place on the way, the swellings may give a false impression of tuberculous adenitis.

The duration of the disease is long, extending over periods varying between months and several years, and in its final stages before the fatal termination, cachexia and dyspnoea are common features. Acute forms are not unknown; they run a septicaemic course and can simulate typhoid. In such cases the organism has been obtained by haemoculture shortly before death. A differential count shows slight leucocytosis and eosinophilia of about 9 per cent. Male adults of middle age constitute the majority of sufferers, and contagiousness, if at all possible, is very weak. Although

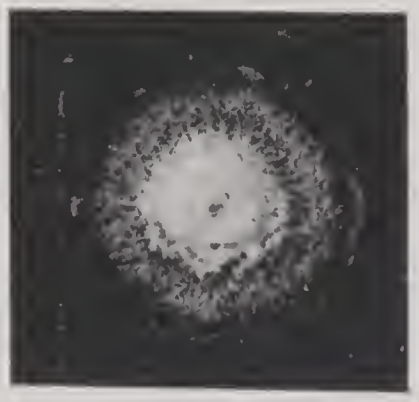


FIG. 22. *Coccidioides immitis*. Colony on Sabouraud 2 per cent glucose-agar. Case of cutaneous lesions of the leg. (Original)

found in animals, evidence is lacking that the disease is transmissible from animal to animal or man or from man to man.

Diagnosis. This can only be accomplished by demonstrating the parasite in infected material or tissue. Cultures and animal

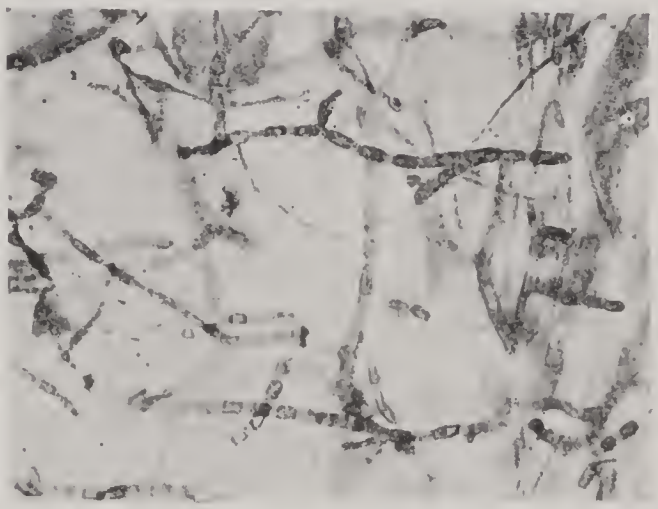


FIG. 23. *Coccidioides immitis.* Cultural morphology. (By courtesy of N. F. Conant)

inoculations, which are generally attended with positive results, clinch the diagnosis. Intradermal tests with "Coccidioidin" are considered specific in diagnosis and are worth trial.

Coccidioides immitis. On Sabouraud glucose-agar, rapid growth, colony cottony, cream-coloured, becoming light brown with age, hyphae 2·5μ in diameter, septate, ramified without conidia, chlamydospores are formed.

Treatment. Rest in bed is an essential condition for any successful treatment. Potassium iodide or other iodine preparations, the mainstay in fungous therapeusis, are ineffective. Some success has followed the administration of tartar emetic intravenously in 1 per cent solutions, vaccines, or colloidal copper intramuscularly. Spontaneous cure is unfortunately exceptional, and in practically all cases surgical treatment ought to be undertaken on accessible parts as soon as a correct diagnosis is made. Evidence of healed lesions of coccidioidal granuloma are, however, recorded in cases dying of other diseases.

FIG. 24. *Coccidioides immitis.* Cultural morphology. 1. racket mycelium, 2. arthrospores, 3. chlamydospores. (Original)

Paracoccidioidosis
Malignant Lymphadeno-Granuloma
Almeida's Disease

This refers to a variety of coccidioidal granuloma in Brazil due to infection with *Paracoccidioides brasiliensis* (Splendore, 1912) Almeida, 1930. Originally observed by Lutz in 1908, the parasite was isolated by Splendore in 1912 from a case of Brazilian blastomycosis with extensive involvement of mucous membrane and a few cutaneous lesions.

In contrast with *Coccidioides immitis*, this parasite attacks the lymphatic glands for preference, but the mucous membrane of the mouth and the intestines are occasionally the sites of the primary infection. Pulmonary and osseous lesions are rare.

Symptoms. The means of introduction into the body is apparently through the digestive tract or the skin. The disease starts, as a rule, in and about the mouth and with hard swellings of the cervical glands. It may remain localized or become generalized by involving the liver, spleen and intestines. It runs a chronic course and usually ends fatally.

Diagnosis. The diagnosis is established by finding the fungus in the sputum or the pus from open lesions. It is present in the tissues as spherical refractile bodies, about 25–40μ in diameter, developing into asci which produce budding spores. These migrate outside the ascus and surround it as exogenous coccoid forms about 1μ in diameter. Asci are unknown in culture, which is as difficult to obtain as are positive results after animal inoculations. When these succeed, localized lesions in the testes are produced. Cultures on serum or ascitic fluid may, however, be tried.

Treatment. The usual medical and surgical measures may be tried, but, so far, no specific remedy has been discovered. Spontaneous recovery in mild types has sometimes occurred.

Paracoccidioides brasiliensis. Slow growth, whitish colonies on Sabouraud media, cottony. In broth and on plain agar tissue forms are obtained, producing a yellowish, wrinkled, cerebriform colony similar to that of *Achorion schoenleini*.

Rhinosporidiosis

Definition. A mycotic infection characterized by the formation of polypoid tumours of the mucous membrane, principally of the nose or naso-pharynx due to infection with *Rhinosporidium seeberi* (Wernicke, 1900).

History and geographical distribution. The parasite was first discovered in 1896 in Buenos Aires by Seeber in a large nasal polypus. Until Ashworth (1923) determined its identity as a fungus of the class *Phycomycetes* it was considered as a protozoon, a *Coccidium* by Wernicke and Seeber, and as belonging to the *Haplosporidia* by Minchin and Fantham. It is found in India, Ceylon, the Philippines, South Africa and in North and South America. Instances of the infection occurring in horses and cattle suspected to be due to the same organism have also been reported from Africa, India and North and South America. The species in animals, *Rhinosporidium*

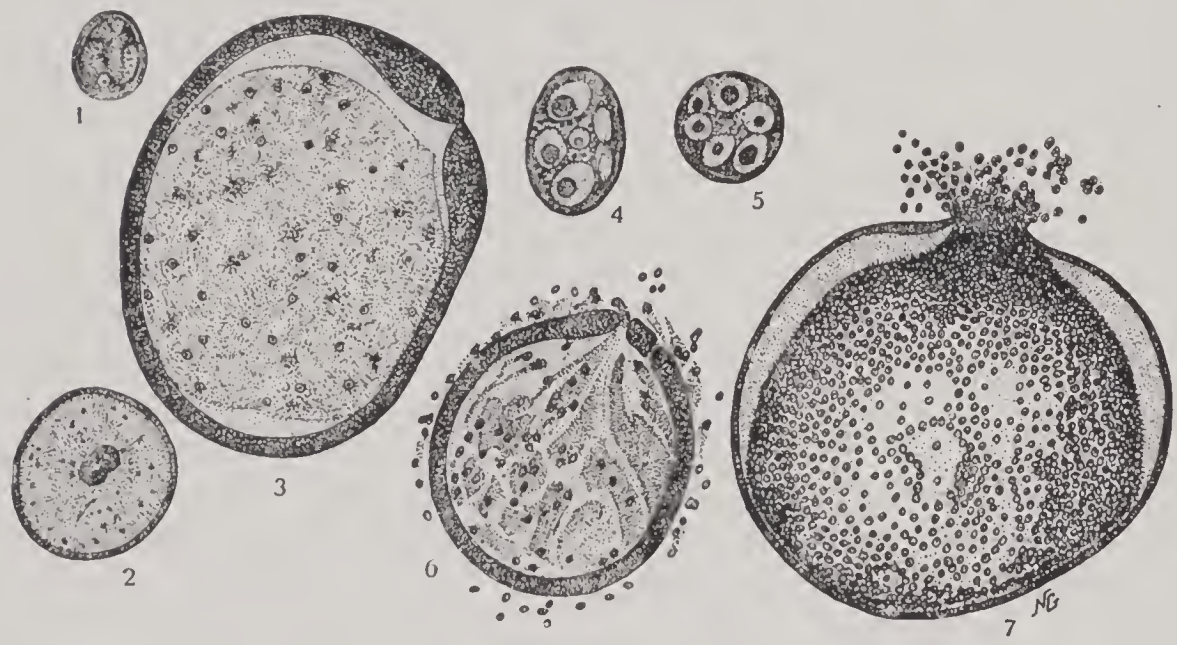


FIG. 25. *Rhinosporidium seeberi*. 1. Early trophic stage, $12 \times 13\mu$, 2. after first nuclear division, about 40μ, 3. section of stage with about 500 nuclei showing beginning of spore and annulus, 4. section of a spore, $10 \times 7\mu$ showing wall, nucleus with karyosome, vacuoles and refringent spherules. 5. similar spore with eccentric nucleus, 6 and 7. ruptured asci. (After Ashworth)

equi Zschokke, 1913, is probably a synonym of *R. seeberi*. First discovered in 1896 in Buenos Aires by Seeber in a large nasal polypus of the horse, its identity as a fungus was determined by Ashworth in 1923.

The parasite in the tissues. The fungus is seen in the polypoid tumours it creates in the form of spherical or oval bodies, ranging in size between 6μ in the youngest representatives and $250–300\mu$ in the older organisms, the mature asci, which are visible to the naked eye in the connective tissue of the tumour. The young cell has a chitinous wall enclosing a vacuolated cytoplasm, a vesicular nucleus and a nucleolus.

For asexual multiplication in the body, sexuality being unknown, nuclear division by mitosis begins in the young forms and is repeated twelve times, the cytoplasm is shared between the daughter nuclei which amount to about 4,000, while the ascus is meanwhile increasing in size. At this stage the wall is thick with deposits of cellulose, except at a point which will serve later as a pore for the discharge of the spores from the fully grown ascus. The cells thus formed finally undergo a twice-repeated subdivision resulting in the production of about 16,000 spores embedded in a mucoid substance inside the ascus.

Each ascospore contains, besides the vacuolated cytoplasm, the vesicular nucleus and karyosome, a few refringent granules of protein reserve material. Rupture of the weak spot on the wall of the ascus liberates the spores into the connective tissue and they are taken up by mononuclear leucocytes and spread by way of the lymphatics to reach fresh areas where they carry on the life-cycle of growth and multiplication. Attempts to cultivate this species seem to have failed so far.

Symptoms. The infection leads to the production of polypoid tumours commonly involving the mucous membrane of the nose or naso-pharynx. Occasionally they occur likewise in the uvula, ear, lacrimal sac and conjunctiva, and a papilloma on the penis has been found to contain the organism. The polypus is cherry-coloured, with whitish spots, the grown asci, is very vascular and friable. The main symptoms are those of mechanical obstruction and irritation of the parts affected, accompanied by an abnormal amount of secretions and perhaps some epistaxis. The parasite has been seen in the mucus from the nose, suggesting a probable source of contagion, but the transmission and contagiousness of the infection remain so far as unknown or inconclusively established points. Children and adults of either sex are equally liable to attack.

Diagnosis. The mycotic character of the polypi can only be ascertained by the discovery of the parasite in the nasal secretions or in the tissues removed by operation.

Treatment. The rich vascularity and friable nature of the tumours render their extirpation with the wire snare a troublesome and sometimes useless undertaking as they have a strong tendency to recurrence. Two per cent solutions of tartar emetic given intravenously every other day, the dose being gradually increased from an initial 0·25 c.c. to 2 c.c., may effect a cure.

Histoplasmosis

Definition. A chronic and fatal granulomatous disease with generalizations in the body causing necrosis of the affected organs and tissues, brought about by infection with *Histoplasma capsulatum* Darling, 1906, or the more recently discovered species, *Histoplasma pyriforme* (Moore, 1934) Dodge, 1935.

History and geographical distribution. *H. capsulatum* was originally seen in the tissues by Darling in Panama in 1906, and *H. pyriforme* was isolated from a case of histoplasmosis in Iowa by

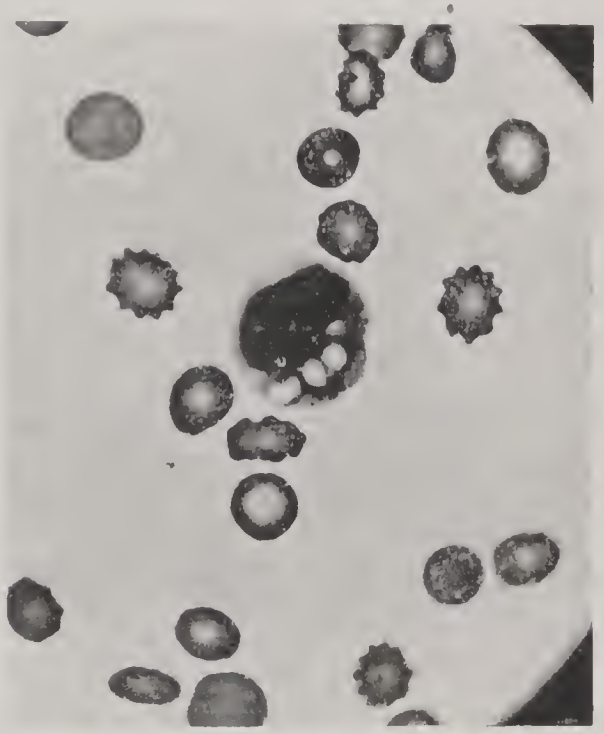


FIG. 26. *Histoplasma capsulatum.* Presence of the parasite in the blood in a mononuclear leucocyte. (By courtesy of N. F. Conant)

Hansmann and Schenken in 1933. *H. capsulatum* was first obtained in culture in 1934 by Monbreun from an infant, a case of Dodd and Tompkins (1934). In 1912, 1913 Rocha Lima described the parasite in the tissues and mentioned its similarity to *Cryptococcus farciminosus* Rivolta, 1873, which produces epizootic lymphangitis in the horse, mule, etc. The disease is so far only known to exist in the United States and Central America; nevertheless, our ignorance of its mode of transmission, reservoir of animal or natural origin, together with its obscure and varied common symptomatology, may be the reasons why it probably passes unsuspected and is erroneously diagnosed in other parts of the world.

The parasite in the body. The parasite is present in abundance in the liver, spleen, lungs and lymphatic glands, or sometimes in the blood as budding yeast-like elements in the endothelial lining of the smaller vessels, in the mononuclear leucocytes and, in heavy infections, in the lymphocytes which also assume a phagocytic function. It is round or oval in shape, 1–4μ in diameter, and possesses a thick capsule. Extracellular forms of the same size have been found only

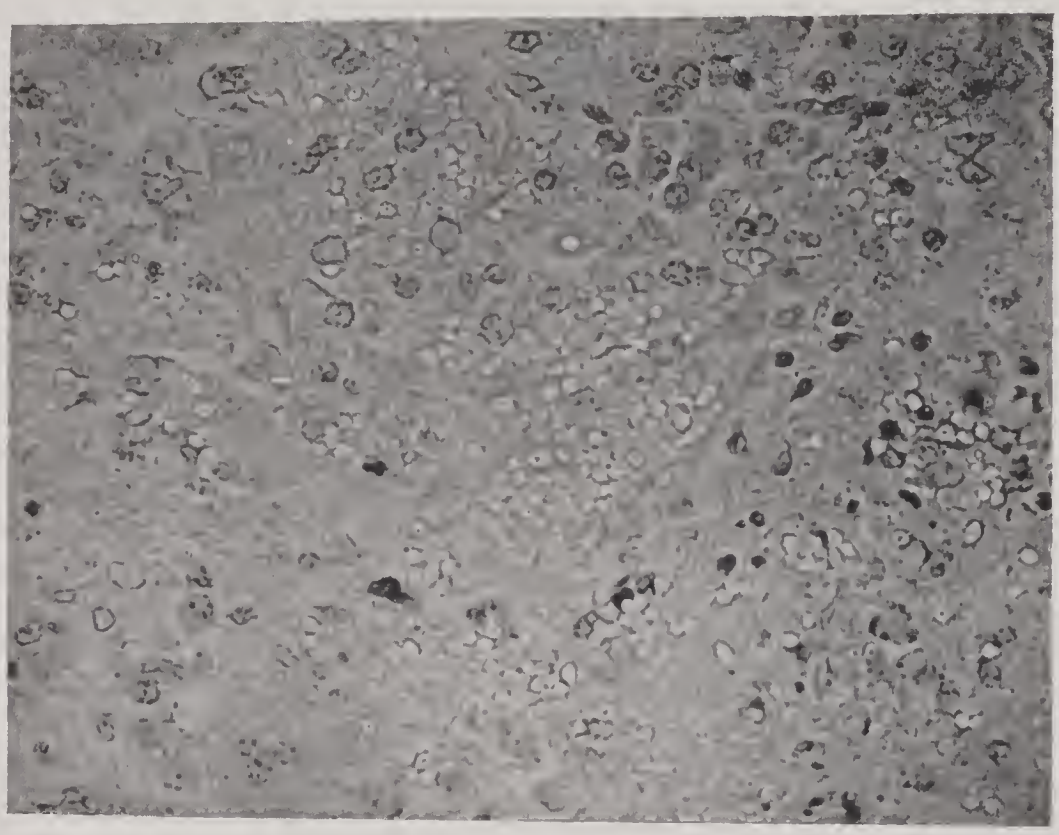


FIG. 27. *H. capsulatum.* Elements of the parasite in the spleen. Section shows the extracellular variety. (Original)

in the spleen and, unlike the intracellular variety, they are surrounded by a clear fairly wide halo.

Morbid anatomy. Necrosis of the infected organs, hyaline degeneration and fibrosis constitute the morbid changes. In the thorax, the lungs show tubercles, some in process of ulceration, while the mediastinal glands are similarly involved and occasionally hydrothorax exists. In the abdominal cavity, splenomegaly, enlargement and cirrhosis of the liver, miliary tubercles of both intestines and enlarged mesenteric and retroperitoneal glands may be seen. A peculiar property of this infection is the absence of suppuration in the cases examined up to the present.

Symptoms. The disease is ushered in by general malaise, lassitude and irregular pyrexia. When fully established, there are symptoms referable to the organs involved accompanied by splenomegaly, often enormous, enlargement of the liver and severe anaemia with marked leucopenia. Gastro-intestinal symptoms of vomiting, diarrhoea or fatal haematemesis, abdominal pain and sometimes ascites may be encountered. Pulmonary implication causes a chronic cough, probably with haemoptysis and signs suggestive of broncho-pneumonia or phthisis.

As a rule very chronic, the disease may be much shortened, and

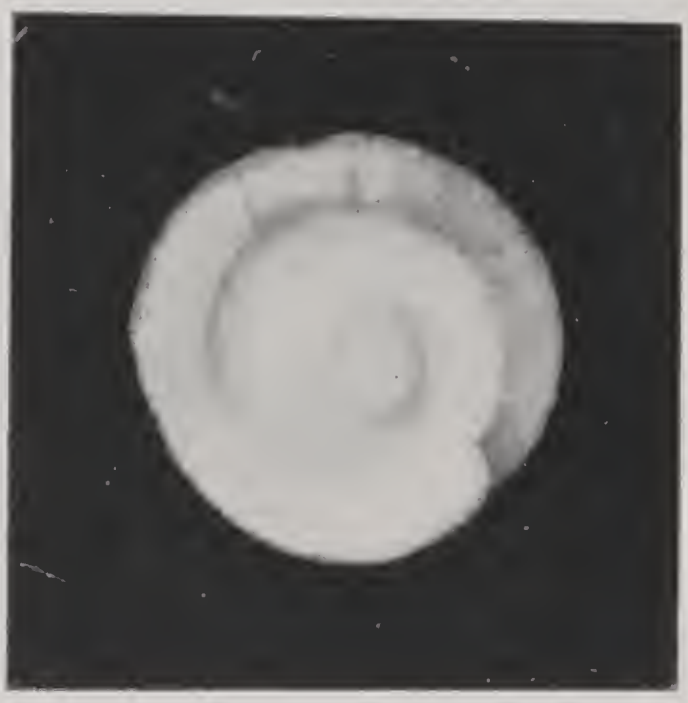


FIG. 28. *H. capsulatum*. Colony on Sabouraud glucose-agar. (After N. F. Conant *et al.*)

the termination is invariably fatal. Adults are generally affected, but Müller in Java and Dodd and Tompkins (1934) in the United States reported the infection in infants. The American case was of an acute character ending in death in about a month from the onset. The organism was seen in mononuclear cells in the blood before the end, and haemocultures were made of it shortly after.

Diagnosis and treatment. Diagnosis is generally made *post-mortem*, and, even if arrived at earlier on clinical grounds, is of little avail as no specific remedy is as yet procurable.

In culture, the saprophytic phase of the organism *H. capsulatum* appears as a white, cottony, poorly growing colony suggesting a pleomorphic species of a dermatophyte. The mycelium is septate, 1–5μ in diameter with lateral

sessile or pedicellate conidia, rarely terminal, round or pyriform, 2–8μ in diameter. Asci are formed, at first smooth, later becoming tuberculate, the tubercles sometimes reaching the size and shape of finger-like processes. A great similarity exists between this species and *H. pyriforme*.

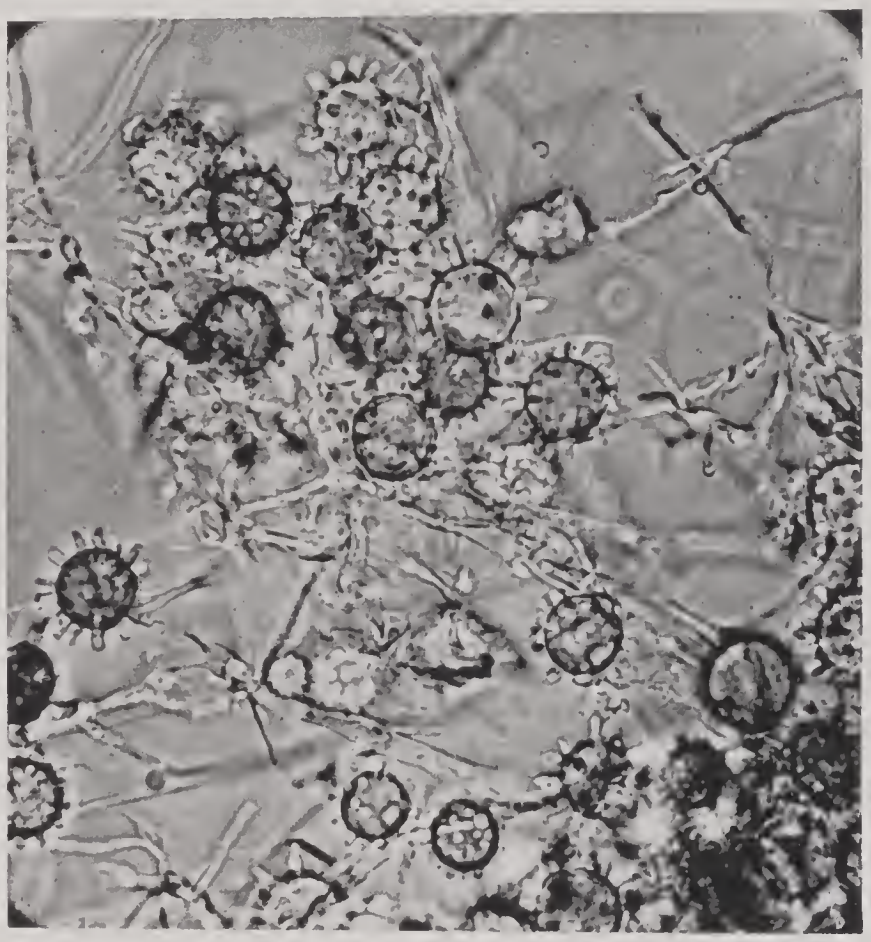


FIG. 29. *H. capsulatum*. Cultural morphology. (By courtesy of N. F. Conant)

Chromoblastomycosis
Dermatitis Verrucosa

Definition. A chronic mycotic infection characterized by the production of extensive granulomatous ulcero-nodular lesions with marked hypertrophy and warty formations usually affecting exposed areas of the skin and the subcutaneous tissue of the upper or lower extremities.

History, aetiology and geographical distribution. The disease probably has an extensive geographical distribution. The South American species *Hormodendrum pedrosoi* Brumpt, 1921, was first isolated by Pedroso in 1911 in Brazil where it commonly attacks workers in coffee plantations. *Phialophora verrucosa* Thaxter, 1915,

is the North American causative organism first reported in 1915 from the United States by Lane and Medlar. Other species of the genus *Hormodendron* responsible for the disease include *Hormodendron langeroni* Da Fonseca, Leão and Penido, 1927, from a

FIG. 30. *Hormodendrum pedrosoi.* Cultural morphology. (Original)

FIG. 31. *H. pedrosoi.* Cultural morphology. (Original)

Brazilian, *H. compactum* Carrión, 1935, from an agricultural labourer in the Island of Puerto Rico, and *H. japonicum* from Japan. The disease has also been recorded from Guatemala, Uruguay and Texas.

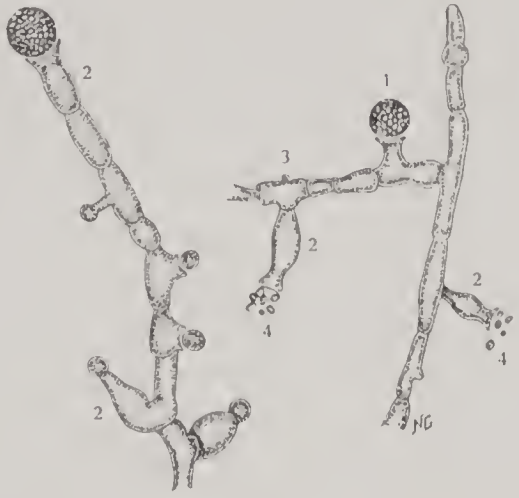


FIG. 32. *Phialophora verrucosa.* Cultural morphology. 1. sporangium-like body. 2. phialides, 3. prophialides, 4. spores. (Original)

In Egypt *Pullularia pullulans* (Bary, 1868) Berkhout, 1923, and *Phialophora verrucose* have been isolated.

Morbid anatomy. The picture presented in sections of the infected skin is similar to that of a reaction against the presence in it of a foreign body. Hyperplasia and hyperkeratosis of the epidermis

is set up, extending deeply into the underlying inflammatory tissue in more or less long tongue-like processes. In this layer of thickened skin the organisms, clustered in groups in the form of cells with brownish walls 3–15μ in diameter, often with internal septation and granular protoplasm, can be distinguished. In the papillae in the superficial layers of the cutis vera more organisms are seen, some incorporated within giant cells, others free and surrounded by leucocytes. The chronic inflammatory process is manifested in this part by typically more than usually dense connective tissue formation, plasma cells, lymphocytes, eosinophiles and polymorphonuclears, epithelioid and giant cells. The number of parasites diminishes as the deeper layer of the cutis vera is reached.

Symptoms. The nature of the disease suggests that the introduction of the fungus, which probably exists saprophytically in the soil, takes place through the skin on a pricking thorn, splinter or other foreign body. It occurs chiefly amongst farm labourers who work bare-footed. Ordinarily, the first signs begin on the dorsal aspect of foot, ankle or toes or on the back of the hand, wrist or fingers. In the earliest stages, the lesions may be nodular, warty, vesicular, pustular or psoriasiform in character, attended with some pain, a variable amount of pruritis and a burning sensation. The eruptions cause no erythematous reaction in the surrounding skin. The focus of infection is usually limited to one area, but a patchy distribution sometimes happens, to be changed in time by coalescence into one uninterrupted surface. Spreading is effected by peripheral extension of old foci, parts of which occasionally heal centrally by scar formation accompanied by a certain degree of atrophy and hyperpigmentation of the skin. By very gradual extension, the diseased part comes to comprise a surface covering most of the back of the hand, fingers and forearm, and on the lower extremity the level of the lesions may reach above the knee and higher.

FIG. 33. Chromoblastomycosis of the leg. (Original)

It takes years for such vast areas to become involved, during which the condition takes on the aspect of almost solid and rough warty tumours covered with whitish crusts, an overgrowth of a

papillomatous nature or raised and scaly verrucous nodules, sometimes ulcerating in isolated spots. With concomitant hypertrophy of the epidermis, swelling and induration of the subjacent soft tissue, the affected part of the limb is increased in size and weight and the diseased surface may attain in some places a thickness of 1 cm. or more. The general health of the patient appears to be totally undisturbed.

FIG. 34. Chromoblastomycosis of the leg. *P. verrucosa* infection. (Original)

Nodules, probably metastatic, containing the parasites, have been found subcutaneously in situations far removed from the site of the disease, on the thigh of the unaffected limb, the forearm and chin. Cases of 15 and 20 years' duration are common occurrences in this seemingly incurable infection. Transmission from patient to contacts is unproven.

Diagnosis. Clinically, an advanced case is often easily diagnosable on sight. Mycologically, the scrapings from the diseased areas show the typical brown fungus bodies as ovoid or spherical cells. The specificity of the different organisms responsible is indistinguishable by a study of their morphology in the tissues, and cultures are the only means of accurate verification.

Colonies of *H. pedrosoi* are black, smooth, adherent and covered with ashy pubescence. Colonies of *P. verrucosa* are of an equally black colour, which pigment is abundantly secreted and imparted to the medium.

Treatment. Potassium iodide may be tried, together with excision in the early stages of the infection. Daily intravenous injections of relatively large doses of sodium iodide over very long periods have met with a certain measure of success. Marked improvement results, and if not sustained, the disease is at least apparently checked. Carrión and Koppisch administered gradually increasing doses

FIG. 35. Chromoblastomycosis. Unusual site of infection due to *H. pedrosoi*. (Original)

FIG. 36. *P. verrucosa*. Colony on Sabouraud 2 per cent glucose-agar. (Original)

FIG. 37. *P. verrucosa*. Cultural morphology. Conidiophores bottle-shaped. (By courtesy of N. F. Conant)

which at the end of the second year of treatment amounted to 9 grammes daily. Other iodine preparations may be tried, but complete recovery is doubtful.

Gilchrist and Stokes' Cutaneous Blastomycosis

Definition. A chronic, contagious infection of the skin inducing the formation of miliary abscesses or nodules which break down into sinuses, fistulae and ulcers and sometimes assume the characters of papillomatous vegetations. The disease, if untreated, is capable of generalization and fatal termination.

History, aetiology and geographical distribution. The parasite is *Zymonema dermatitidis* (Gilchrist and Stokes, 1898) Dodge, 1935 (synonyms, *Blastomyces dermatitidis* Gilchrist and Stokes, 1898, *Endomyces dermatitidis* (Gilchrist and Stokes, 1898) Moore, 1933, etc.). It exists as a saprophyte in nature and has been isolated from dung. In 1894 Gilchrist and Stokes discovered it in America, causing chronic subcutaneous lesions in the form of abscesses and ulcers. More cases, also from America, where it seems to be of common occurrence, as well as from Europe and elsewhere, have been observed since. *Scopulariopsis americanus* Ota, 1928, and *Monosporium tulanense* (Castellani, 1928) Agostini, 1932, are, according to Ota and Kawatsure (1933), two additional aetiological agents capable of producing the same picture of Gilchrist's blastomycetic dermatitis.

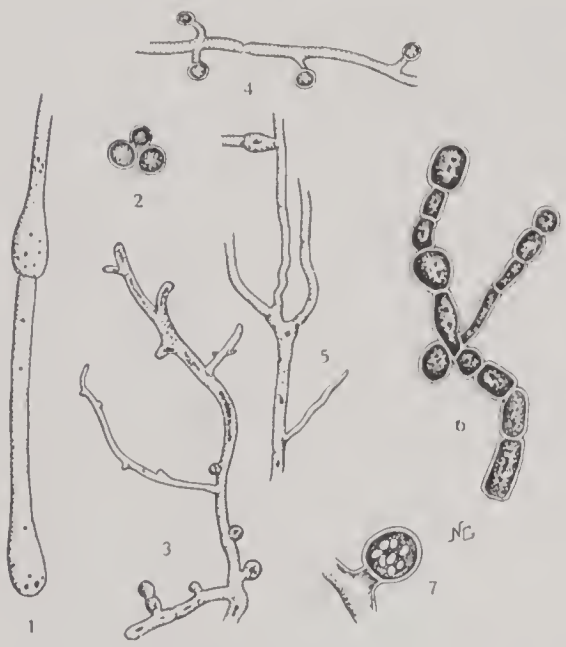


FIG. 38. *Zymonema dermatitidis*. Cultural morphology. 1. racket mycelium, 2. budding cells, 3. and 4. mycelium and lateral conidia, 5. ramified mycelium, 6. chlamydospores, 7. ascus. (Original)

The parasite in the tissues. In the lesions the parasite, according to Moore (1933), occurs as spherical or ovoid budding cells 7–12μ, or rarely 20μ, in diameter, separate or in small groups. The protoplasm is reticulated, granular and often vacuolated, with a nucleus and is enclosed in a thick refractile capsular wall. Mycelium, sprout-cells and asci with ascospores are formed in culture.

Morbid anatomy. The changes seen in sections of cutaneous lesions are hyperplasia of the epidermis with tongue-like downgrowths into the corium which, like the rete mucosa, is infiltrated with polymorphonuclear and young connective tissue cells. In the rete the cells are swollen, and beside the leucocytic infiltration, epithelioid and giant cells are found incorporating some of the parasites. Periarteritis and endarteritis with occasional obliteration of the lumen may likewise be present.

FIG. 39. Blastomycosis of the nose. (Original)

Symptoms. Presumably the fungus is introduced through the skin or by inhalation. The initial signs manifest themselves as slowly growing, small, hard papules or nodules which coalesce, soften and then break down into abscesses, fistulae and elevated ulcers with yellowish crusts, and the picture may have the aspect of papillomatous growths. The lesions are painless and usually occur on the face or extremities, but they may begin anywhere on the body, more often than not over the site of a cut or abrasion.

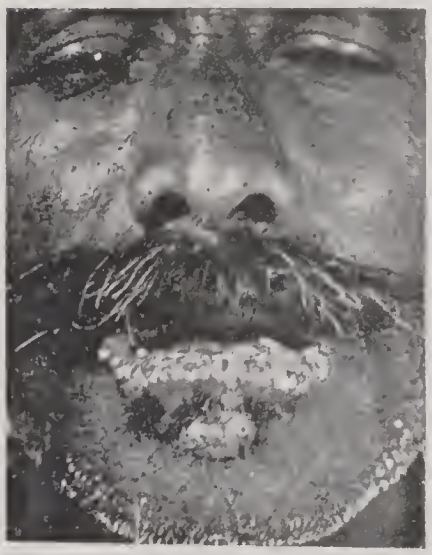


FIG. 40. Cutaneous and mucous membrane blastomycosis of mouth, lips and skin neighbourhood. (Original)

Local extension, auto-infection in scratching when there is occasional pruritis, and invasion of fresh localities by mestastases via the blood-stream or the lymphatics, ultimately lead to generalization of the disease resulting in the formation of multiple subcutaneous abscesses in different parts of the body and the implication of deep-seated structures and organs. The great majority of cases are of the cutaneous type, but primary lung infection is possible, and the condition closely simulates pulmonary tuberculosis until the appearance of secondary miliary abscesses belies that diagnosis. The lymphatic glands are not as a rule enlarged.

Contagion is admitted as quite possible by inoculation of the parasite from the lesions through some breach of surface. Adult

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males and females of any age may be attacked, while the literature on the subject includes no instances of the infection in children. The disease is of slow evolution and the prognosis, especially in untreated cases, is bad.

Diagnosis. The cutaneous manifestations of the infection are likely, at some time or other, to present false pictures of lupus, cold abscesses or verrucous tuberculous lesions. Tertiary syphilis, molluscum contagiosum, malignant growths, mycetoma or other blastomycoses are more erroneous labels for this disease.

The presence of yeast-like organisms in the pus, sputum or in

FIG. 41. Cutaneous blastomycosis. Sinuses on nose, cheek, soft and hard palates. Cured by internal iodine administration and local iodine dressings. (Original)

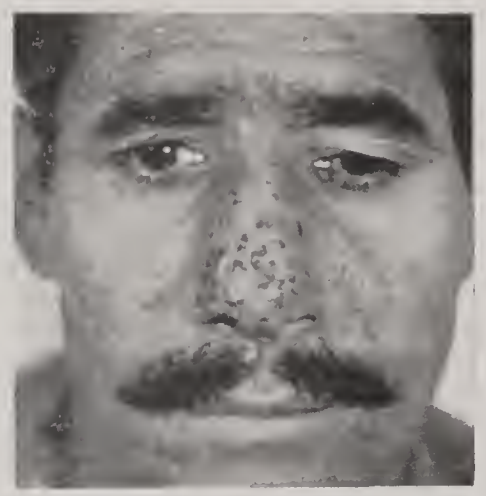

FIG. 42. Case illustrated in Fig. 41. After treatment. Note levelling of lesions and healing under scabs. (Original)

small portions scraped from the lesions determine the fungous nature of the infection. The isolation in culture of the specific cause will clinch the diagnosis.

Cultures of *Z. dermatitidis* are humid, whitish to chestnut, translucent, elevated, rugose, covered by an ashy layer of aerial hyphae bearing pyriform conidia about 5μ in diameter on short sterigmata.

Treatment. Potassium iodide given over a very long period and local dressings with a weak iodine and potassium iodide solution are the usual means at our disposal. Surgical interference, though effective, has probably the disadvantage of disseminating the organisms.

Blastomycosis Glutealis Fistulosa
Kartulis' Gluteal Blastomycosis

Kartulis (1909) described a cutaneous infection of the gluteal region in a series of Egyptian cases in Alexandria, and referred to the causative organism which he isolated as "Saccharomyzetaceen," thus recognizing its blastomycotic nature. It occurs in culture as ovoid or elongated cells, up to 18μ in length, singly or arranged in chains; chlamydospores are seen, and ascus and ascospore formation

FIG. 43. Gluteal blastomycosis (clinical diagnosis). *Schistosoma mansoni* ova discovered in discharge. (Original)

is claimed to take place during its evolution. Synonyms of the parasite include "*levure de Kartulis*" (Sasakawa, 1922) and (Ota, 1924), *Cryptococcus kartulisi* (Castellani, 1928), and *Myceloblastanon kartulis* (Ota, 1928). The valid name, however, appears to be *Castellania kartulisi* Dodge, 1935, in a genus erected by the latter to comprise the group *Monilia*, as well as yeasts with poorly-developed mycelium, and of which only inadequate morphological descriptions exist.

Symptoms. The infection is characterized by the production of indurated nodes in the skin of the gluteal region. By slow evolution they soften and break down into abscesses, sinuses, and later into

fistulae burrowing deeply into underlying fibrosed subcutaneous tissue and exuding thin and scanty pus. The patients are generally males of middle age of the poorer hospital classes. It is probable that direct contact of the buttocks with the soil, considering the habits of the local farm labourers, squatting postures, etc., may play a rôle in the introduction, through abrasions sustained somehow on the skin, of the infecting agent.

Ali Ibrahim (1930) described a type of lesion in Egyptians bearing a great deal of resemblance to Kartulis' so-called blastomycosis. Compared with this, it is met with among the better class of patients

FIG. 44. Kartulis' gluteal blastomycosis.

and attacks the true skin, selecting that of the scrotum, inguinal region and perineum, sometimes extending to the inner aspect of the thigh, or to the pubis and lower abdominal surface. The gluteal areas, when implicated, are generally final points of spread. Another site of election is the axilla, whence it may creep down to the sides of the chest. Initial globular swellings burst open in time and form abscesses, and eventually sinuses and fistulae discharging a little pus are produced. Treated surgically, fresh sinuses usually break out in the incisions.

Since Kartulis' time there has been no record of a repetition of his results until recently when the author, after investigating eight cases presenting Kartulis' syndrome, found in four instances yeast cells in the lesions and obtained the specific organism in culture.

In one case only, the clinical picture presented a deviation from the classical description in the production, after the nodular stage, of large ulcers about 3 cm. in diameter, with undermined edges and granulating floors. These ulcers had as much tendency to spontaneous cure and recurrence as to response to local treatment. Healing left fibrosed, pale pink, smooth patches. Two other cases gave negative results, both by direct examination and by culture of the discharge from the lesions. The seventh yielded *Fusarium solani* (Mart., 1842) Appel and Wollenweber, 1910, proven non-pathogenic to guinea-pigs and probably a contaminant. In the

FIG. 45. Kartulis' gluteal blastomycosis. (Original)

material from the eighth and last patient, *Schistosoma haematobium* ova and miracidia were seen. In a country where schistosomiasis is prevalent, and in the type of patient who is a potential victim to that infection, a bilharzial aetiology for infections in Kartulis' area should be borne in mind, at least from the point of view of differential diagnosis.

Other species isolated from abscesses in the gluteal region include:

Syringospora cutanea Dodge, 1935 (=*Myceloblastanon cutaneum var. Takahashi*, 1929); from gluteal, perineal, inguino-crural and axillary areas; also from the neck of an infant.

Saccharomyces zimmeri Dodge, 1935; from the gluteal region and upper thigh.

The parasite in the tissues. A great similarity exists between the cultural elements of the organism in its saprophytic stage and its

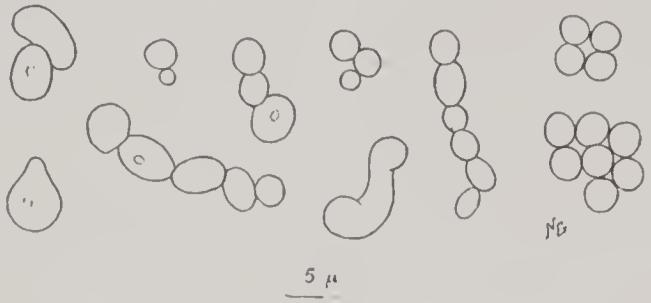

FIG. 46. Gluteal blastomycosis. Elements of Kartulis' yeast in the discharge from the lesions. (Original)

appearance in the tissues. Here it occurs as yeast cells, rounded, about 2–5μ in diameter, in chains of budding cells of two to eight, as groups of three or seven, or as elongated pear-shaped or distorted dumb-bell-like cells, up to 10μ in length. Refractile bodies are seen in some cells.

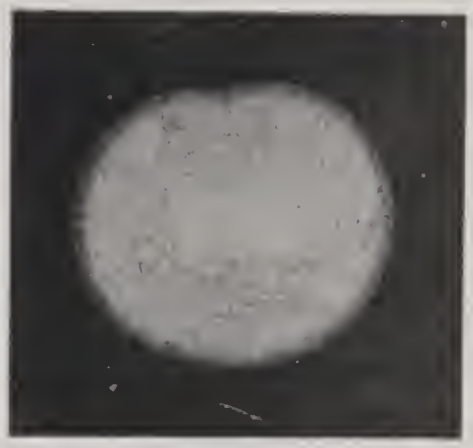

FIG. 47. Colony of Kartulis' yeast on 2 per cent glucose-agar. (Original)

Diagnosis. The identification of the above elements in the lesions may be regarded as sufficient evidence of blastomycosis, especially after confirmatory cultures.

Treatment. Local antiseptic dressings with iodine or dyes is indicated, and surgical measures with subsequent skin grafting may have to be entertained in some cases. In the absence of mycotic findings, and

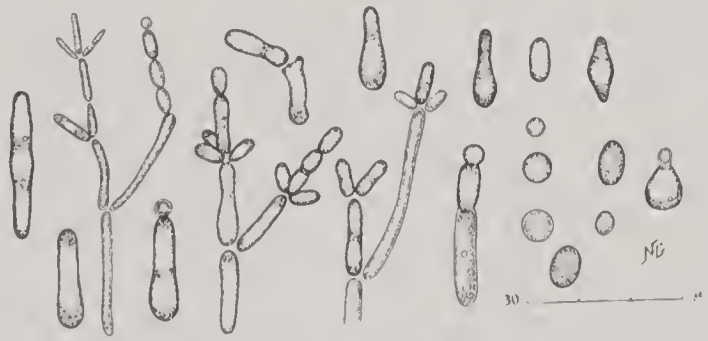

FIG. 48. *Castellania kartulisi.* Cultural morphology. (Original)

assuming a bilharzial condition, antimony therapy may be tried together with local treatment. Ultra-violet rays may be helpful.

Blastomycosis of the Central Nervous System

Definition. The condition recognized and best described under this heading is referred to as "Torula Meningitis," causing cystic blastomycosis of the cerebral grey matter. Freeman (1931) reviewed the subject and gave a comprehensive account of the infection, its aetiology, symptoms and morbid anatomy.

History, aetiology and geographical distribution. Stoddard and Cutler first reported this infection in 1916 in the U.S.A., where it mostly occurs, although European and Asiatic cases are on record. It would seem that its rarity in other parts of the world is largely due to failure to diagnose it.

Frothingham (1902) isolated from the lung of a horse *Cryptococcus histolyticus* Stoddard and Cutler, 1928 (=*Torulopsis histolyticus* Castellani and Jacono, 1933). Experimental inoculation with this species in 1916 by Stoddard and Cutler reproduced the cerebral cystic lesions of Torula meningitis in man caused by *Cryptococcus meningitidis* Dodge, 1935 (=*Torula histolytica* Harrison, 1928). Dodge supplied the name of this species which comprises for convenience a number of strains isolated by Harrison from human cases. No adequate description so far exists of the organism, stress having always been laid by authors on pathological and clinical features of the infection to the exclusion of any cultural study of the species isolated. In Stoddard and Cutler's experimental work Frothingham's old species from the horse was employed, and although typical cerebral lesions were reproduced in animals, this cannot rightly be taken as proof of the specificity of the parasite in man, especially as they did not attempt to grow the organism from their human cases.

Mycotic involvement of the central nervous system is not, however, confined to infection by the above species, as it may be brought about through the agency of other organisms. It may occur primarily or in the course of a systemic blastomycosis however produced. Primary infection of the meninges and spinal cord have been caused by *Coccidioides immitis*, and *Zymonema capsulatum* (Dodge and Ayers, 1929) Dodge, 1935 has been isolated from granular nodules on the surface of the medulla in a case diagnosed as meningoencephalitis complicating pulmonary tuberculosis. The cerebro-spinal fluid was free from evidence of infection in this latter case, and on *post-mortem* examination the cerebellum, pons, medulla, cranial nerves and an old scar on the thigh were found covered with these

nodules of mycotic origin. Among other instances, thrush, when generalized, may rarely implicate the brain. *Actinomyces asteroides*, found, among other situations, in meningitis, was originally recovered from a case of pseudo-tuberculosis with cerebro-spinal meningitis.

Morbid anatomy. The avenue of infection is probably the respiratory tract and through the sinuses. The meninges become affected and the infection travels thence along the perivascular sheaths to the cortex and may sometimes reach the white matter. Both cerebral and cerebellar lesions are encountered. The meningitis which is of the granulomatous type is usually basal and bears a close resemblance to tuberculous meningitis. The meninges show discrete or generalized granulomatous lesions which, histologically, are composed of endothelial hyperplasia, fibrosis and small-celled infiltration, as well as giant cells with numerous organisms.

Deeper spread of the infection appears in the sub-arachnoid space and in the ventricles where the fluid becomes by degrees turbid, slimy or even of a gelatinous consistency. The morbid process may reach the cortex which is involved in 50 per cent of the cases, and has blisters with clear, turbid or gelatinous contents as well as organisms. Deeper still, the white matter may finally become implicated and presents mottling or fissures. These changes are occasionally associated with evidence of inflammation. Capillary emboli of organisms play a large part in the production of fresh foci.

Symptoms. The infection manifests itself insidiously in the form of headaches of gradually increasing intensity and frequency which are accompanied by stiffness and pain in the neck and limbs and, occasionally, by gastric or respiratory disturbances. Later on, mental aberration of varying degree and quality, insomnia and other symptoms suggestive of increased intracranial pressure are developed. These may variously be ascribed to brain tumour, encephalitis or meningitis. Pyrexia is absent and the course of the disease is a slow one, characterized by extreme emaciation and invariably terminating fatally.

Diagnosis. Budding round cells with a thick gelatinous coating may be detected in the cerebro-spinal fluid after centrifugalization. Some of the sediment is mixed with a drop of chinese ink and examined under the microscope. There is usually no evidence of inflammatory reaction. Morphologically similar cells, except for

the surrounding gelatinous coating, may be obtained on culture, while filament and ascospore development is absent.

Cryptococcus meningitidis colonies on malt extract agar are white, shiny, becoming yellow, then brown. Cells spherical, 3·5μ in diameter, with oil globules. On glucose-agar, colonies of *Cryptococcus histolyticus* are at first whitish, then yellowish, thick, pasty and shiny. Cells spherical, some sprouting, 1–6μ in diameter, with thick capsules.

Clinically, the nearest approach to diagnosis is a recognition of a cerebro-spinal condition. Its more specific nature may, however, only be ascertained after examination of the cerebro-spinal contents and by culture.

Treatment. No treatment, curative or even enough to check progress of the infection, has hitherto been successful. Palliative measures, however, may be attempted. Repeated lumbar puncture for reducing intracranial pressure gives relief, and general hygienic and dietetic methods should be adopted to combat as much as possible the wasting which is so marked during the later stages of the disease.

Busse-Buschke's Generalized Blastomycosis

Busse and Buschke (1893) discovered the parasite *Atelosaccharomyces hominis* (Vuillemin, 1902) Froilano de Mello *et al.*, 1918 (synonyms, *Cryptococcus hominis* Vuillemin, 1902, etc.) in a woman in Germany. She presented painful, ulcerating, subcutaneous gumma-like nodules, adherent to the skin and the underlying tissues on the face and neck. Later she developed subperiosteal suppurative nodules on the tibia. With progressive generalization, internal organs, eye, cervical and axillary glands and ribs became involved. A short time prior to her death the parasites were found in the cerebro-spinal fluid. The disease ran a slow course, with occasional exacerbations and some pyrexia, and the general health was affected.

On *post-mortem* examination it was found that the invasion of bone had produced subperiosteal suppuration and intra-osseous abscesses with extensive necrosis and cavity formation. The ulcerating cutaneous lesions showed on section a peripheral zone of reactionary inflammatory tissue including the parasites in giant cells. One point of note was the absence of reaction in the ribs and spleen which, nevertheless, contained some parasites.

In the pus and the inflamed tissues, the organisms existed in a free state or enclosed in giant cells in the form of round or oval budding cells with thick double-walled capsules, mostly in small

groups which appeared to be surrounded by a homogeneous gelatinous envelope. This species is easily grown and produces neither mycelium nor ascospores in tissue or culture. The forms obtained in culture are identical with the cells in the pathological material except for the absence of the mucilaginous sheath around the grouped parasites. Most media are favourable for culture, preferably at 38°C. Multiplication by sprouting. Neither mycelium, asci nor spores are seen.

The infection may be confounded with tertiary syphilis, tuberculosis, leishmania, other blastomycoses, etc., but the microscopic

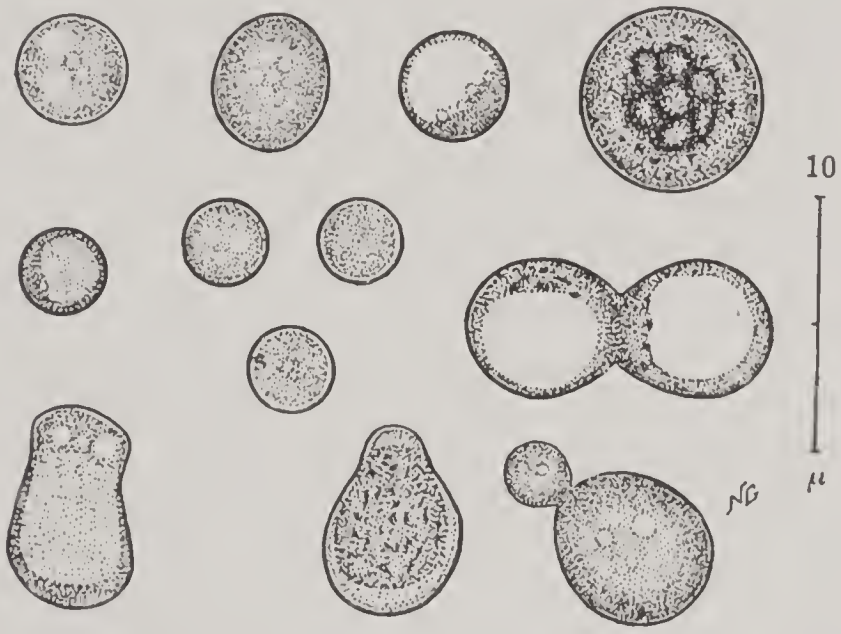

FIG. 49. *Cryptococcus hominis*. Cultural morphology. (Original)

demonstration and the cultures of the causative organism clear the diagnosis.

Treatment. Palliative measures only are possible. Iodide and other lines of therapeusis may arrest further spread of the parasites.

Laboratory Diagnosis of Yeasts and Yeast-like Fungi

Sputum, pus, stools, etc. Spread smears on slide with or without a drop or more of water according to consistency, and examine fresh or stained with strong Lugol's iodine (iodine, 1 gramme; potassium iodide, 2 grammes; distilled water, to 100 c.c.).

Yeast cells and pseudomycelium stain a light brown, while vacuoles and fat droplets in the cells assume a darker shade. Sections and teased portions of tissue may be stained with Gram.

Cultures are made on a 2 per cent glucose-agar (plates for preference). Pick yeast colonies from contaminants and re-inoculate. Bacterial contamination may be eliminated after one or two passages through Raulin's solution.

Filamentization of the *Blastosporineae* is obtained at 37°C. on poor media. Asci and ascospores also appear under these conditions, but may take weeks to form. Gorodkowa's medium is used for this purpose.

CHAPTER V

MYCOSES OF THE DIGESTIVE TRACT

General Survey

The mouth, leading as it does into the digestive tract, and incidentally to the lungs, serves as a portal through which intercommunication is almost continually sustained between the exterior with its multitudes of fauna and flora and the long intestinal canal traversing the body which, remarkably enough, seldom fails to cope with extraneous intruders. These organisms, mostly originally saprophytic, may occasionally take on a parasitic mode of existence, especially with the aid of previously instituted infection, disease or injury. Accordingly, fungi rarely induce morbid changes along the digestive tract, notwithstanding their various representatives which, from time to time are isolated, either where no deviation from the normal is apparent or occasionally in connection with visible abnormalities. In these cases the species collected by culture are nearly all members of the groups of yeasts and yeast-like organisms, as well as a few isolated *Actinomyces*, all of which produce benign changes, if at all. There are, nevertheless, the group of cases where the mycotic infection has a tendency to generalization with serious enough results and implication, among other organs, of the intestines and liver.

The mucous membrane of the mouth, including the palates, fauces, uvula and pharynx, may, in addition to creamy stomatitis and patches of thrush, show superficial greyish lesions and ulcers. In some instances there is an accompanying bronchomycosis. Yeasts and yeast-like species are the common offenders, and the usual throat symptoms are in evidence. Tickling and burning sensations, dysphagia and an irritable cough, sometimes accompanied by copious expectoration, constitute the main list of possible complaints, and there is as a rule a diffuse inflammation of the areas involved which may be coated with greyish or whitish plaques. Spread of infection to the larynx, epiglottis and arytenoids is also recorded. Acton (1919) reported an epidemic amongst soldiers in Mesopotamia, from which *Actonia* (*Endomyces*) *tropicalis* (Acton, 1919) Dodge, 1935, was isolated. The lesions produced were in the nature of

creamy, slightly adherent patches and widespread inflammation implicating the whole throat. Extension of the infection to the bronchi and bronchioles ended in some patients with fatal pneumonia.

The tongue has its share of fungi, which have been grown from cases of thrush, sprue and black pilose tongue, all of which are described elsewhere. Besides the aetiological agents of these conditions, *Sporotrichum* has been isolated from ulcers, and *Actinomyces* from abscesses of the tongue. From carious teeth, it is interesting to note, *Actinomyces* has been recovered, flourishing presumably merely as a saprophyte.

Species considered to be strains of *Actinomyces bovis* were found in granules in the crypts of both normal tonsils, and in others with tonsillitis and abscess formation. In some cases pin-head, hard, white or reddish lesions as well as ulcers have yielded *Sporotrichum*, while yeasts and yeast-like species produce thrush patches, curdled milk spots of a superficial nature, or these may occur without visible signs of their presence inside the tonsillar crypts. In a few instances mycotic lesions of the tonsils appear as complications in the course of typhoid fever, quinsy, bronchomycosis, etc., and occasionally tonsillomycosis has been followed by pulmonary symptoms due probably to the same aetiological agent in the throat.

Thrush is recorded from the oesophagus and stomach and balls of mycelium have formed in the latter organ from which red yeasts have also been obtained on culture of material withdrawn for biochemical investigation.

Liver involvement occurs in generalized blastomysosis or other mycotic infections that become disseminated, and a species of *Actinomyces* has been grown from liver abscess. The possibility of intestinal mycosis, apart from its occurrence in generalized infections, is entertained in connection with the different species obtained from diarrhoeic and dysenteric stools.

Fungi in the Intestines

If it is to be assumed that diarrhoea or dysentery of mycotic aetiology exists, as judged by the number of species isolated from abnormal stools, careful consideration will show that such an assumption is based on inconclusive evidence. The first and main objection lies in the fact that a multitude of species, yeasts and yeast-like organisms apparently may constitute a normal part of the flora of the intestinal canal where they induce, in the majority of cases, no morbid

changes and are easily procurable on culture of stools selected haphazard for this purpose. Moreover, the unproven pathogenicity of most of these species adds further point to the objection.

Secondly, when a review is made of the known causes of diarrhoeas and dysenteries of varying degrees, the case against mycotic infection of the intestines is strengthened. Protozoal, spirochaetal and helminth infections rank foremost in the aetiology of dysentery. Avitaminosis, food and other poisonings, the usual intestinal diseases, faulty feeding in children, hot weather disturbances, etc., all give a syndrome, sometimes only varying in degree, which is liable when undiagnosed by careful investigation and exclusion to be attributed to fungi when they are isolated from the abnormal motions in these conditions. Contamination from the air and the strong likelihood of the innocent presence of these very same organisms prior to the onset of the intestinal symptoms are seldom taken into account.

This side of the picture as it is presented has, however, a reverse aspect in a few cases which may be accepted as authenticated, and include generalized blastomycosis, histoplasmosis and paracoccidioides infection involving the intestines. *Actinomyces* has been isolated from the vermiform appendix and thrush organisms are reported from the faeces in advanced cases of this infection.

Lingua Nigra Pilosa
Black Pilose Tongue

Definition. A benign, chronic affection, probably mycotic, characterized by hypertrophy and dark-brown or black discoloration of the papillae of the tongue.

Aetiology. The possibility of this infection being a true mycosis is as yet a debatable point in spite of the discovery of mycelium or yeast-like cells on and in the papillae. Against the definite acceptance of the mycotic theory is the failure, in one particular survey, that attended the attempts to obtain cultures from at least most of the long series of cases examined. Moreover, the experimental inoculation of laboratory animals either proved the non-pathogenicity of the incriminated organisms or did not reproduce the tongue lesion.

A list of the species isolated so far is given below, with some of their respective properties and histories, as well as a few comments.

Rhizopus niger (Ciaglinski and Hewelke, 1893) Barthelat, 1903.

Discovered in 1893 by Ciaglinski and Hewelke in three cases, and later, on two more occasions by Sendziak in 1894. Thermophobe species, thriving best at 25° to 27° C. and ceasing to grow at 37° C. Present on the pathological coating produced on the papillae, which would be of a lower temperature than the tissues of the organ itself. Non-pathogenic to rabbits or guinea-pigs.

Acremoniella atra Corda, 1837, isolated in Egypt.

Castellania linguae-pilosae (Lucet, 1901) Dodge, 1935.
Synonyms: *Saccharomyces linguae-pilosae* Lucet, 1901;
Cryptococcus linguae-pilosae Castellani and Chalmers, 1913, etc.

Isolated from a fair number of cases since Lucet first investigated it. Cellular double-walled elements, 3–6μ in diameter, present in and on the papillae. Temperatures between 25° and 35° C., fruit juice or glucose media most favourable for growth, ferments sugars and acidifies the media. Predisposition to infection probably established through gastric affection and acidity of mouth. ? Reproduction of lingual lesion successful on tongue of rabbit. Pathogenic for mice.

On most media growth white, creamy, shining or somewhat dull, tomentose. Cells spherical, 4–8μ in diameter, or elongate 12–17 × 6μ, occasionally in short chains up to 10 cells, which in old cultures have small ovoid protrusions attached by five pedicels to them. In some cells the contents divide into five to six unequal masses grouped at the periphery. Each mass is surrounded by its own wall.

Actinomyces guegueni (Ota, 1928) Brumpt, 1921.
Synonyms: *Oospora lingualis* Guéguen, 1908;
Nocardia guegueni Ota 1928, etc.

Isolated by Guéguen from a case of black tongue, together with *Castellania linguae-pilosae*, which may be considered to be the causative organism. Bacillus-like elements, 0·5μ in diameter, present in the papillae. Pathogenic for the guinea-pig.

Oospora catenata Schaede, 1934 and *O. fragilis* Schaede, 1934.

Two incompletely described species reported from black tongue.

Atelosaccharomyces catanei Dodge, 1935.
Synonym: *Cryptococcus sp.* Catanei, 1925.

Isolated from black pilose tongue, also in association with *Castellania linguae-pilosae*. Non-pathogenic for guinea-pig or rabbit.

Cryptococcus cooperi Dodge, 1935.
Synonym: *C. quasi linguae-pilosae* Cooper, 1932.

Isolated from one single case out of a series of 102 black tongue patients. Pathogenicity not reported.

The condition is apparently allied clinically and pathologically to thrush and is due to saprophytes which accidentally take root and thrive, even on a limited scale, in unhygienic mouths offering favourable substrata. *Castellania linguae-pilosae*, nevertheless, seems to deserve more than light consideration from the point of view of specificity as it has been isolated more often than any of the other species.

Symptoms. The lesions are the same, regardless of the causative organism. Dark brown or black, round or slightly irregular patches, discrete or confluent, and of various dimensions cover the conical and lenticular papillae usually on the oral portion of the dorsum of the tongue anterior to the V-shaped *sulcus terminalis*, but the pharyngeal portion may also be infected. Hypertrophy of the involved papillae is a marked feature, accompanied by degeneration of the surface epithelium.

FIG. 50. *Lingua nigra pilosa.* Both dorsum and pharyngeal part affected. Villate and filiform papillae over a central patch are atrophied. (Original)

Diagnosis. The discoloration and the site of the lesion are the clues in clinical diagnosis. Microscopical examination of scrapings from the patches will reveal short lengths of mycelium and arthrospores or yeast-cells. Positive cultures confirm and determine the aetiology.

Treatment. This is conducted on the same lines as for thrush. Lugol's iodine as a mouth-wash three time a day is also effective.

Thrush

Definition. A cosmopolitan blastomycosis affecting, under certain conditions, infants, debilitated or senile subjects, characterized by the formation of milk-white or gray patches chiefly on the buccal mucosa, but other situations are occasionally similarly involved.

History. The disease is old-established and has been known since the time of Hippocrates and Galen as *stomata aphthodea*, *aphtae infantum*, *Saphino*, *Soor*, and other clinical names, and more recently as *aphthous stomatitis*, *muguet*, *stomatite crémeuse*, etc.

Langenbeck (1839) was probably the first to recognize the fungus in the lesions, but Berg (1842) was more positive in pointing out their mycotic nature, and gave a description of the yeast. Robin (1847) contributed a fuller account of the parasite and named it *Oidium albicans* in 1853, and further investigations by different authors have since confirmed this and brought to light the existence of more than the one species as responsible for the infection. The plurality of the aetiological agents is now an admitted fact, although a tendency

still persists, especially in medical literature and practice, to call in an academically loose fashion all the yeast-like organisms of thrush by the classical name.

Aetiology. The following is a list of species isolated from cases of thrush:

Syringospora albicans (Robin, 1853) Dodge, 1935.
Synonyms: *Oidium albicans* Robin, 1853;
Syringospora robini Quinquaud, 1868;
Saccharomyces albicans Reess, 1877;
Monilia candida Plaut, 1885;
M. albicans Zopf, 1890;
Endomyces albicans Johan-Olsen, 1897;
Candida albicans Basgal, 1931;
Mycotorula albicans Langeron and Talice, 1932.
Zymonema albicans (Okabe, 1929) Dodge, 1935.
Synonym: *Endomyces albicans* Okabe, 1929, isolated from a long series of cases of thrush in Japan. Pathogenicity proven.
Castellania metchnikoffi (Castellani, 1916) Dodge, 1935, isolated in London.
C. loudinensis (Castellani and Chalmers, 1919) Dodge, 1935.
C. metaloudinensis (Castellani and Chalmers, 1919) Dodge, 1935, isolated from mouth and vagina.

There is a great likelihood that more species and strains of the same organism are capable of producing the infection, but owing to the difficulties in the determination of yeasts in general, the organisms encountered in thrush are often summarily dismissed as (*Oidium albicans*).

From a practical point of view, and because of the uniformity of the morbid process, diagnosis, prognosis and treatment, this is perhaps a harmless procedure and may only be criticized on academic grounds.

Syringospora albicans in the lesions. The parasite exists in the membranes to which it gives rise in the form of simple or ramified pseudomycelium of elongated cells attached end to end, 3–5μ in diameter, some of the filaments possessing terminal swollen spherical or ovoid cells, wrongly referred to as chlamydospores. Blastospores, spherical or ovoid, terminal or nodal, are seen on the pseudomycelium and its branches. The patch is composed of pseudomycelium in between, and blastospores inside the epithelial cells uniting them into a membrane, while some of the destroyed mucosa in the form of débris adds to the general mass.

Predisposing factors and mode of infection. It may be stated that the infection is contagious but only under certain conditions. The exposed tissue must have an acid reaction and the individuals must otherwise present a vitality lowered by infectious fevers, exhausting diseases or senility, or be subjects of some favourable

digestive tract disturbance, for the parasite and its various strains are facultative and have been isolated from the mouths of healthy persons. In Berlin, Langenbeck (1839) noted the lesions of thrush in typhus patients, a common enough sequel, easily understood by the acidity of the saliva in that fever, as proved by Calmette in 1893. Quinquand (1868) had to moisten the tongue first with lactic acid before he could reproduce thrush by human experimental inoculation.

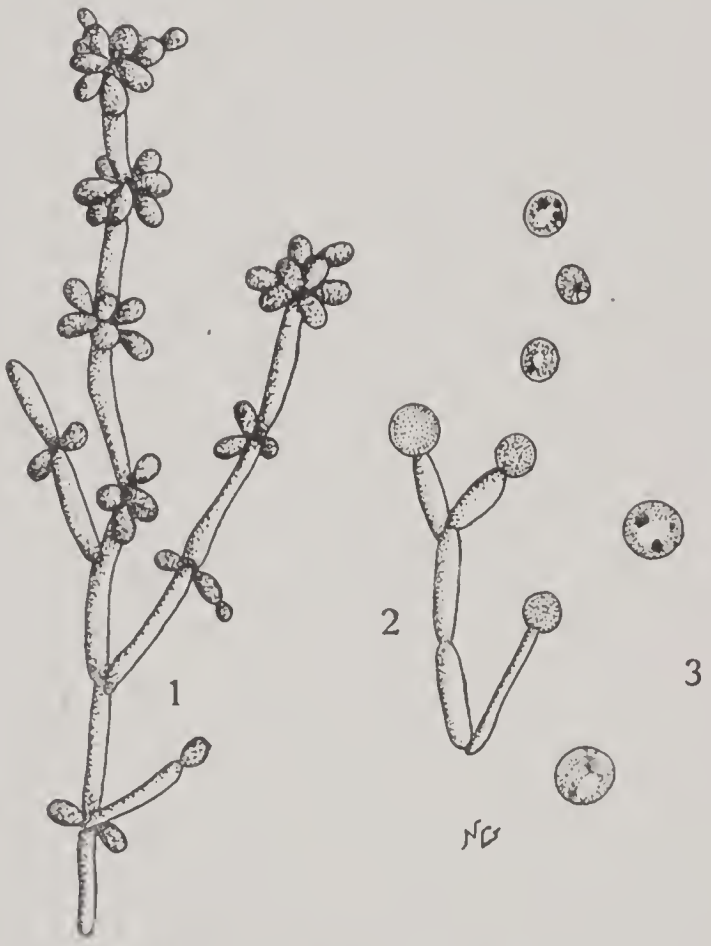

FIG. 51. *Syringospora* (*Monilia*) *albicans*. Cultural morphology. 1. simple regularly spaced verticils, 2. terminal chlamydospores, 3. cells with vacuoles and metachromatic granules. (Original)

Infants, especially the bottle-fed ones, constitute the majority of sufferers chiefly among the poorer classes in the midst of unhygienic and neglected conditions. The infection may be contracted from the nipple of the mother, the teat or the interior of the bottle, or possibly directly from the air, the receptivity of the baby having been prepared by a pre-existing diarrhoea, rickets or other infantile debilitating states.

Symptoms. The typical lesions are preceded by an erythematous stomatitis which marks the stage of implantation of the pseudo-

mycelium in the epithelial layer of the mucosa. This initial stage is characterized by soreness and is followed, usually on the second day, by hyperaemic patches which mark the sites of implantation of the fungus. With proliferation of the parasite and the consequent destruction of cells, raised roundish areas surrounded by a red ring, at first cream-coloured, changing later to a dirty greyish hue, are formed in various situations in the mouth. They generally appear on the third day and assume different shapes and dimensions attaining a thickness of 1–2 mm. or more. The sites of election are the lateral aspects, dorsum and tip of the tongue, with hypertrophy of the underlying papillae, the mucous membrane of the cheeks and the gums. The membrane is adherent at first but becomes less so in time and can be removed mechanically, leaving red, raw and slightly bleeding surfaces underneath, on which fresh formations soon appear, or they may ulcerate. By coalescence and extension, the lips, the soft palate, uvula and tonsils may be invaded, and less commonly, the lesions may reach the pharynx, oesophagus, stomach and intestines. Primary involvement of any of the three latter sites is possible though a rare occurrence, and other uncommon localizations of thrush include the vulva, vagina and the urethra. *Syringospora albicans* has likewise been isolated from parotid pus, the nipples of nursing mothers, moist skin folds, the glans of a diabetic patient, tuberculous cavities and other aberrant situations.

The affected mouth is usually dry, tender, and painful on sucking or swallowing. Beyond that, there is little else except what is caused by the co-existing condition which favoured the appearance of thrush.

Diagnosis. This presents little or no difficulty clinically, as the signs are pathognomonic. The organism may be grown in culture to determine its identity.

Syringospora albicans grows best on slightly acid glucose-agar. Colony smooth, creamy white, sometimes with irregularly arranged little heaped areas, or with deep furrows. The component elements are mostly blastospores but filamentous forms may occur in old cultures. More filaments of pseudomycelium are obtained in liquid media with divisions disposed in simple verticils, regularly spaced, terminal and nodal. Terminal " chlamydospores " may be encountered.

Glucose, laevulose and maltose are fermented and sucrose only after inversion by the acids formed. Sugar reactions are essential for specific determination.

Treatment. Treating the general health of the patient as well as any co-existing nutritional disease is of foremost importance, and this includes vitamin A and D therapy. For the local condition,

it stands to reason that the reaction of the mouth should be changed to alkalinity. To this end, the accessible membranes can be wiped off by means of a piece of cotton wool or some clean soft material moistened with a solution of borax (gr. X to ℥ j) or with glycerin of borax. Sodium bicarbonate is equally as effective, and sodium borate may be administered internally to anticipate extension of the lesions to the rest of the digestive tract. Alkaline douches are recommended for vulval or vaginal thrush.

Sterilization of the bottle in the case of bottle-fed infants, and wiping the nipple clean with the borax solution before the feeds, and the child's mouth afterwards, are necessary procedures both in treatment and prophylaxis.

Sprue

Definition. A chronic, mainly tropical, wasting disease, characterized chiefly by lingual lesions, marked intestinal fermentation and the passage of bulky, pale-coloured, diarrhoeic, frothy motions, and complicated by a pernicious type of anaemia with occasional exacerbations of symptoms.

History. The earliest clear account of the disease was given by Hillary of Barbados as far back as 1766. Later publications include Manson's in 1880, in which he accurately described the disease and called it "sprue"—a modification of the Teutonic *sprouwe*, *spreu* in Scotland, etc., for thrush. Independently in the same year, Van der Burg in Batavia entitled it *Indische spruw*. "White tropical diarrhoea" of Sir John Fayrer (1881) and "psilosis" of Thin (1897) are among the numerous names used by different authors in their reference to the condition which, by their combined studies, eventually came to assume the status of a new and recognizable clinical entity with uniform features and course instead of one of the common diarrhoeas that it was hitherto considered to be.

Geographical distribution. Essentially an affection of tropical climates, sprue is by no means absent from temperate regions. Hot weather, but not necessarily excessively high temperature, seemingly acts as a favourable factor in its progress. It is very prevalent in Central America, the West Indies, and to a lesser extent in the south of the United States. Other endemic centres include Ceylon, India, Southern China, Korea and Japan, the Philippines and Australia, making up as it were a circumference embracing the Malayan Archipelago and some more islands where the disease is also rife. The occurrence of sporadic cases in Europe is not unknown.

Aetiology. Immoderate indulgence in drink and the wrong type of food for hot climates, sedentary occupations, unsuitable forms of recreation or sport carried to a strenuous pitch, late hours and such routine as is unavoidably or otherwise imposed by local conditions and social intercourse in the tropics, probably act as predisposing factors inasmuch as they tend to lower the individual's resistance. Blame is likewise laid at the door of insufficient protein and vitamin intake, brought about by partial or total exclusion from the diet of meat, vegetables, fruit and dairy produce which had to make way for more remunerative, if less essential, agricultural crops in some areas.

Apart from the above, sprue has been considered as a syndrome, an inadmissible hypothesis in the light of its typical symptoms and course. The interpretation that the term covers bacterial and protozoal varieties appears unjustified: the bacteria cited have not been proved as direct causes, and similarly, the organisms of dysentery, spirochaetes and helminths, notably *Strongyloides stercoralis*, suggested as possible aetiological agents should be dismissed as pre-existing or superimposed parasites.

Scott's theory of low serum-calcium, based upon the analogy between the symptoms of sprue and those of diseases due to calcium deficiency, as well as the hypothesis of general glandular insufficiency are well supported by chemical analysis and clinical and other findings. The great similarity that exists between the blood pictures of sprue and pernicious anaemia coupled with Elder's definite interpretation of sprue as a deficiency disease in 1920, led Bloomfield and Wychoff in 1927 to attack it with success on the same principle applied by Minot and Murphy (1926) of replacing the deficiency in pernicious anaemia by means of liver. The mycotic theory of infection is due to Kohlbrügge (1901) who was the first to observe yeasts in sprue stools. This was taken up by Castellani, Ashford and others, until Ashford (1914) in Porto Rico described a Monilia which he consistently isolated from the tongues and stools of sprue patients. Ashford's high percentage of positive cultures of his *Monilia psilosis* against the comparatively low incidence of that fungus in healthy subjects or in other affections deserves consideration. The fact that that species has also been isolated from buccal sprue lesions is significant; yet the possibility of its being a strain of *Monilia albicans* of mouth, intestinal and vaginal thrush is not too remote. The organism may have existed prior to the development of sprue or may equally be a superimposed invader of a field previously made suitable for its reception. The difficulty of picking out

causes and effects from among the different manifestations of the disease is ever present. So far the deficiency theory is holding its own, although liver therapy which causes disappearance of all sprue symptoms has to be maintained and the old dietetic treatments undertaken at the same time if relapses are to be avoided.

The isolation of the following species from sprue patients, and of several more besides from diarrhoeic stools, accentuates the doubtful nature of the purely mycotic explanation and the specificity of *Monilia psilosis*.

Syringospora psilosis (Ashford, 1917) Dodge, 1935.
Synonyms: *Monilia sp.* Ashford, 1915;
M. psilosis Ashford, 1917; isolated *post-mortem* from intestines, Egypt;
Parasaccharomyces ashfordi Anderson, 1917;
Myceloblastanon psilose Ota, 1928;
Mycotorula psilosis Langeron and Talice, 1932;
Candida psilosis Almeida, 1933.
Isolated in Puerto Rico, pathogenic to rabbits and guinea-pigs.

Parendomyces vanderburgii (Kohlbrügge, 1901) Dodge, 1935.
Synonym: *Oidium vanderburgii* Kohlbrügge, 1901.
Isolated in the Dutch East Indies.

Castellania decolorans (Castellani and Low, 1913) Dodge, 1935.
Synonyms: *Monilia decolorans* Castellani and Low, 1913;
Myceloblastanon decolorans Ota, 1928.
Isolated from the tongue.

Geotrichum rotundatum (Castellani, 1912) Almeida, 1933.
Synonyms: *Endomyces rotundatus* Castellani, 1912;
Monilia rotunda Castellani and Chalmers, 1913;
Monilia rotundata Castellani, 1914;
Oidium rotundatum Castellani and Chalmers, 1919;
Mycoderma rotundatum Brumpt, 1927;
Myceloblastanon rotundatum Ota, 1928;
Candida rotundata Basgal, 1931.

Pathology. In fatal cases the body as a whole presents a state of general wasting apparent as much in the muscles as in the internal organs. Atrophy of the latter is a striking feature; the liver, spleen, kidneys and adrenals, heart, etc. are found anaemic and some of them greatly reduced in size. Fatty degeneration of the liver and Kupffer cells in some cases, and instances of fatty and granular degeneration of the cells of the pancreas with fibrosis in and between the acini are occasionally discovered. Of special interest is the condition of the bone-marrow, which shows varying degrees of aplasia or hyperplasia of its elements, the changes sometimes being typical of pernicious anaemia.

The pathological findings in the small intestine in the majority of cases are degeneration of villi, glands and follicles, producing small

superficial ulcerations of the mucosa, together with marked atrophy of the muscular coat amounting almost to transparency. The ileum is usually the more deeply involved portion of the bowel, but the damage may be widespread, extending to the caecum and colon, and gastric and duodenal erosions may be found. There is, nevertheless, no peculiarity by which the morbid condition could be specifically ascribed to sprue.

The tongue lesions are characterized by destruction and desquamation of the surface epithelium and atrophy of the fungiform and filiform papillae, but some of the former may, on the contrary, appear swollen and prominent. Patches of thrush on the buccal mucosa and pharynx, a certain amount of inflammation and even ulceration may be present in the upper part of the alimentary canal implicating the palate, fauces, tonsils and oesophagus.

Symptoms. The mode of infection or the extent of the incubation period are so far unknown. An early history is often elicited of chronic digestive disturbances vaguely interpreted as dyspepsia which takes the form of anorexia, nausea and sometimes vomiting, heartburn, flatulence, and constipation alternating with occasional attacks of morning diarrhoea. With further progress of the disease the patient complains of palpitation, anaemia, emaciation, asthaenia and such nervous manifestations as cramps in the legs and numbness of the extremities, and he develops a general irritability and some psychic changes. At the same time there are evanescent attacks of discomfort in the mouth and tongue amounting to a little rawness and tenderness and the formation of vesicles on the mucosa which, however, heal spontaneously. Aknephaskopia or twilight blindness and other ocular symptoms, including mydriasis, keratitis and disturbances of accommodation, are amongst the prosprue manifestations. It is to be borne in mind that these are symptomatic of vitamin D_2 deficiency. Failing libido in men and some menstrual irregularities in women generally conclude the list of complaints in the earlier stages.

The subject presents a more or less wasted appearance with the skin hanging loose over his emaciated body, a muddy complexion, sometimes bearing patches of brownish pigmentation on the face and neck, pale conjunctivae and perhaps a trace of jaundice. Superficial blisters and erosions on the sides and tip of the tongue are signs usually observed from time to time during an exacerbation. The organ looks red, is perhaps thrown into folds from swelling of its mucous membrane, and the inflammation, extending to the

fungiform and filiform papillae, produces the aspect described as "strawberry tongue." Patches of thrush may also form on the buccal mucosa and may involve the palate, fauces and pharynx.

This state of affairs would continue throughout a period of months or years interrupted by intervals of comparative quiescence which stop after indiscretions in diet or drink, physical or sexual over-taxation, chill or other causes, until by degrees the typical clinical picture of sprue supervenes.

When the disease is fully established the characteristic oral and intestinal symptoms are intensified every time a lull is broken by an exacerbation. The soreness of the mouth and tongue is aggravated by unduly salty or acid food and drink, and is accompanied by excessive salivation, painful mastication and dysphagia, especially when, as an occasional complication, the oesophagus is involved. The motions are unusually copious, frothy but may be formed, pale grey in colour, fatty (fatty acid crystals, high proportion of split fat, as well as soluble and insoluble soaps), foul-smelling and acrid, the acidity, together with the soluble soaps, inducing a burning sensation in rectum and anus, felt mostly during the act of defaecation. Extension of the infection by contiguity from anus to vagina with consequent vaginitis in females is another likely complication. The intestinal symptoms may, at a given time, coincide with those of the tongue, or the two may alternate; a flare-up of the lingual condition abates, only to be succeeded by an intestinal bout. Apparent limitation of the disease in that way to one or other set of symptoms has been referred to as "tongue sprue" and "intestinal sprue," two misnomers each of which merely describes a predominant part of a whole, while the remainder is in abeyance.

The final picture is a manifold exaggeration of the earlier condition in all its details. The lingual lesions now implicate all the anterior two-thirds of the organ, which from repeated recurrences becomes reduced in size and hardened. Desquamation of the epithelium and atrophy of the papillae give it a glistening and smooth appearance during a respite, and the aspect of raw beef while an exacerbation lasts. The excessive irritation to the sore tongue and mouth by food and drink, except the blandest, drives the patient almost to fasting. The diarrhoea becomes a constant and distressing symptom, and the anaemia, the worst feature which invariably accompanies the disease, even if it does not cause it as some authors hold, assumes a pernicious character. The emaciation maintains its progress and may reach extreme degrees, reducing the body in

some cases to as little as, or even less than, half its former weight. Visceroptosis, as a result of loss of mesenteric fat and atrophy of the abdominal muscles, superficial ulcerations in the stomach and duodenum simulating gastric and duodenal ulcers, and proctitis and haemorrhoids produced by the irritating diarrhoea, are later complications which help to add to the patient's sufferings. Sooner or later he enters into a cachectic stage which terminates in death, occasionally hastened by an intercurrent infection.

On clinical examination, the patient presents no individual pathognomonic features. Apart from the lingual lesions, the progressive anaemia and loss of weight are very apparent in the sallow dry loose skin, through which the bony prominences stick out, and in the reduced size of the abdominal organs which can hardly be palpated. Viscesroptosis, flatulent abdominal distension, oedema, weak and rapid pulse, functional cardiac murmurs, petaechial haemorrhages and patches of pigmentation in the skin, in fact most of the changes to be expected in severe anaemia, nutritional disturbances, intestinal toxaemia and wasting diseases, can be observed.

Of the diseases which may have pre-existed and come to the fore because of weakened resistance, tuberculosis ranks high. Dysentery, which has been incriminated as a basis for sprue, judging by the common coincidence of the two conditions, malaria, syphilis, helminth infections, etc., are further instances of possible associated diseases which tend to make matters worse.

Sprue, as a general rule, attacks adults between 20 and 40, but practically no age is immune and the two sexes are nearly equally susceptible to infection. From racial and sociological points of view the white community in the tropics, especially the females and the natives in more affluent circumstances, constitute the majority of sufferers, the incidence being peculiarly highest in towns.

The course of the disease is very chronic. Under adequate treatment, however, amelioration or even cure of the lingual and intestinal symptoms can be attained, but there are instances where the disease as such is not thereby arrested and continues to a fatal termination. In other cases, on the other hand, the anaemia disappears with the elimination of the organism from the stools. A latent form is occasionally observed in Europeans in an apparently healthy condition who develop sprue for the first time years after their return from the tropics. In others who had already contracted it, residence in colder climates is punctuated by freedom from symptoms in the winter months and relapses during the warm weather.

Diagnosis. The reduced size of the liver and spleen, the characteristic diarrhoea and the condition of the tongue are regarded as cardinal signs for suspecting sprue, especially in conjunction with increasing anaemia and emaciation and the tendency of the symptoms towards sudden appearance and disappearance. Demonstration and culture of the yeast-like organism from the tongue and faeces affords strong confirmatory evidence.

For pure culture of *S. psilosis*, part of the stools is emulsified in distilled water or, for preference, in ox bile to which is added 20 per cent glycerin. A drop of the emulsion is then spread in streaks on plates of 4 per cent glucose-agar glycerinated to 20 per cent and of *p*H 6·3.

Colony cerebriform, smooth, chalk white, cells spherical or ovoid or irregular and polymorphic. Giant cells common, spherical, 3–5μ in diameter with oil droplets. Pseudomycelium 2–5μ in diameter, up to 1 mm. in length.

Further investigation reveals a reduction of haemoglobin which may be as low as 20 per cent, a poor number of red cells, a tendency towards leucopenia, frequent cases of poikilocytosis, anisocytosis and polychromatophilia and, in rare instances, the presence of normoblasts, especially megaloblasts. The blood picture is at first that of a hypochromic microcytic anaemia which later becomes megalocytic and hyperchromic, showing evidence of regeneration. Reduced serum-calcium is likewise a common finding.

Analysis of the gastric and duodenal contents shows varying degrees of achylia in the stomach, while high acidity and reduction in amylase and lipase may be discovered in the duodenum. In the stools, a pronounced excess of fatty acids over neutral fats is usually present, accompanied by the normal quantity of bile-pigment, but the element bilirubin is reduced in the intestine to leucobilin and urobilinogen, hence the pale colour of the motions.

Differential diagnosis. The earlier syndrome of sprue is difficult to label in a satisfactory manner and is often vaguely blamed on to the climate. With the establishment of the fully developed disease, however, several affections may have to be excluded. The diarrhoea is likely to be mistaken for that of dysentery or for intestinal tuberculosis, and the lingual lesions may be ascribed to tertiary syphilis, tuberculosis or other less serious affections, while the association of diarrhoea with the condition of the tongue might suggest pellagra or Addison's disease. A consideration of the history and physical signs of sprue, appropriate laboratory investigations, the absence of blood and mucus from the stools, the pyrexia of bacillary dysentery,

the cutaneous and nervous manifestations of pellagra, together with the discovery, in some cases, of *Syringospora psilosis* in the lesions of the tongue or in the faeces, should help in differential diagnosis.

Chronic malaria and hookworm infection, common as they are in the tropics, constitute additional sources of error which are, nevertheless, avoidable by microscopical examination. The digestive symptoms might, on rare occasions, point to gastric or duodenal ulcer, both of which could be ruled out by radioscopic and chemical tests, or to chronic pancreatitis. In the latter case the neutral fats in the stools, contrary to what happens in sprue, will be found greatly in excess of the fatty acids. Lastly, the co-existence of one or other of some of the infections detailed above is a possibility which should always be borne in mind.

Treatment. In this connection, Ashford's conclusions from his wide experience of sprue cases show that regulation of the diet is an essential factor if a favourable issue is to be expected. A liberal regime, sugar- and cereal-free, from which fats are eliminated—to all intents and purposes a diabetic diet—and a strict milk regime are recommended to suit the requirements of both early and late cases respectively.

An absolute milk diet should not be inflicted indiscriminately on all patients, for "There must be potent reasons," Ashford points out, "for employing a starvation diet in a disease where symptoms are the result of tissue starvation and exhaustion." Milk, monotonous as it is, is reserved for later stages when lingual and intestinal symptoms are at their worst or during exacerbations. Fortunately, priceless alternatives for milk are provided for patients who fail to tolerate it in Cantlie's "Meat Cure," Van der Burg's "Fruit Cure," and in the "Strawberry Treatment" of Thin. On the other hand, the "Liberal Sprue Diet" elaborated by Ashford is indicated in the earlier stages of sprue and may also be gradually introduced to replace milk after it has been in force for a few weeks and has effected some improvement.

The liberal sprue diet. Sugars, carbohydrates and fats in all forms are prohibited in this diet, which should be calculated at not less than 1,800 calories a day. The fungus which presumably plays a part in the aetiology of the disease is thereby starved without interference with the average needs of the body. Perseverance for months on end is the key to success, and relapses are not necessarily a sign of failure. They may be dealt with by reduced rations for a day or

two in bed after a small dose of castor oil, which measures usually check the symptoms and allow return to the fuller regimen. With the liberal diet the patient's routine activities are not hampered, an obvious advantage in the majority of cases.

The milk diet. In more advanced cases, as well as when attacks of severe tongue lesions and intractable diarrhoea are sustained, confinement to bed, an aperient, and milk, to the exclusion of everything else, are indicated. A daily allowance of a litre and a half to start with, gradually increased to about four litres, is distributed over several meals to be sipped through a straw. This diet is generally followed in the second week by marked amelioration, but must be continued for some weeks after the disappearance of the last symptoms. When this is achieved, fruits, vegetables, and finally the liberal diet are gradually made to replace the milk. If the stools, which should be inspected daily, show evidence of poor digestion, this may be corrected as suggested by Ashford, by the addition to each meal of two ounces of banana flour gruel.

The meat diet. Patients who cannot tolerate milk and cases with extreme degrees of diarrhoea derive a great deal of comfort and benefit from Cantlie's meat regimen which, incidentally, must under no circumstances bec ombined with milk. About two pounds of rump-steak or fillet, finely chopped and stored in the refrigerator, constitute a daily ration to be divided over six meals. For each meal a portion is made into patties, lightly grilled or seared in a buttered saucepan, and eaten hot. A week of this is generally attended by decided improvement, but the patient can no longer fight a growing loathing for meat, which should then be gradually substituted by the liberal diet. Rich meat or chicken broth may occasionally be given to break the monotony.

The fruit diet. Under this treatment, small frequent feeds of fruit with a low acidity are prescribed, the amount consumed being gradually increased to several pounds a day. With the advent of a favourable change, the liberal diet is introduced.

Medicinal treatment. To counteract the acidity and make up for the reduced digestive ferments the following prescription has been found of definite value in sprue:

℞ Pancreatin
Takadiastase āā 15
Magn. Oxid. 25
Calcii Carbonat. 50
M. et divide in chart. No. 50
Sig.—One powder three times daily after meals.

Sodium bicarbonate in large doses, 2–3 ℥ t.i.d., in addition to the dietetic treatment, lessens the acidity of the intestinal contents and inhibits the growth of fungi of the *Monilia* type in the stools. The buccal and lingual lesions are dealt with by means of glycerin and borax and alkaline mouth washes.

An acid strychnine mixture as a general tonic and the following mixture for checking too frequent bowel movement have proved useful in Ashford's hands:

℞	Tinct. Opii Deodorat.		4
	Bismuth. Subnitrat.		
	Cret. Præparat.	āā	13
	Syrup. Acaciae		100
	Aq. Cinnamom.		200

Sig.—One tablespoonful two-hourly until relief is obtained.

Against the anaemia, liver extract is recommended by Ashford in the dysplastic cases as a routine, but on the whole, reliance on drugs, except in special circumstances, should be avoided. Attention is directed to diet, rest, both mental and physical, and to general hygienic measures. Wherever possible, return to a more favourable climate ought to be considered and attempts towards toning up the wasted body and increasing the resistance by foods rich in vitamins, and such means as massage, helio- and hydrotherapy are generally productive of good results.

Manson first obtained the knowledge of the value of liver therapy in sprue from native Chinese doctors. Elders (1920) was the first to lay down the concept that a deficiency state was responsible for the syndrome of sprue. Bloomfield and Wyckoff (1927), applying the same principles in sprue as Minot and Murphy (1926) in pernicious anaemia, by replacing the deficiency by means of liver, met with success. The disappearance of symptoms under high liver diet or liver extracts parenterally is very encouraging despite the necessity in some cases of maintaining its administration at least in smaller quantities to forestall relapses.

To correct vitamin deficiency more specifically, riboflavin and vitamin B complex are given, especially folic acid which has recently proved very effective. Sulphaguanidine may help to abort the diarrhoea as the normal intestinal flora may assume a pathogenic character in the abnormal alimentary tract.

CHAPTER VI

SPOROTRICHOSIS : HEMISPOROSIS

Sporotrichosis

Definition. A chronic mycotic infection characterized by the production of disseminated gumma-like lesions often liable to be confounded with syphilomas and tuberculomas, closed or ulcerating, involving dermis, subcutaneous tissue, mucous membrane or deeper structures, or of localized nodules with lymphangitis along the course of the vessels draining the affected part.

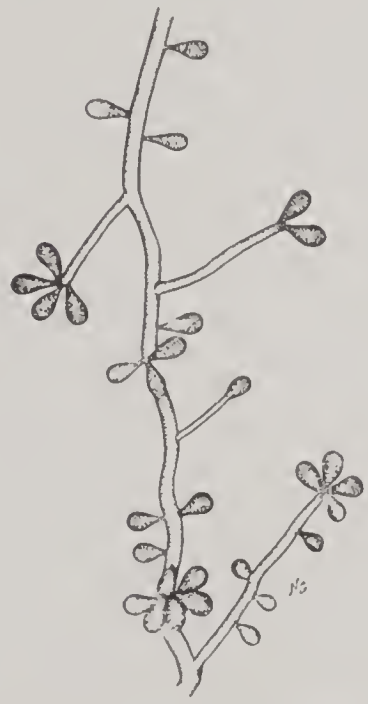

FIG. 52. *Sporotrichum schencki.* Cultural morphology. (Original)

Aetiology, history and geographical distribution. Schenck was the first to record the disease in 1898 from America in a patient with subcutaneous abscesses. Hektoen and Perkins (1900) published a report of more cases, also in the United States, and de Beurmann, Ramond and Gougerot (1903–1914) followed with further instances in France and thoroughly investigated the infection, its pathology and the parasite in the lesions. Other workers have since continued to contribute to our knowledge of the mycosis and of its aetiological agents in different parts of the world.

The classical species causing sporotrichosis is *Sporotrichum schencki* (Hektoen and Perkins, 1900) Matruchot, 1910 (synonym, *Sporotrichum beurmanni* Matruchot and Ramond, 1905) occurring in several of the South American states, in Algeria, Madagascar and in the United States, especially in the Mississippi and Missouri valleys. It has also been found in wild rats in Brazil, in horses and mules in Madagascar, and in horses in the United States. This organism has also been isolated from onychomycosis.

Other species causing the same or clinically similar lesions are the following:

Actinomyces dori (de Beurmann and Gougerot, 1906) Brumpt, 1927, isolated from subcutaneous abscesses.

Sporotrichum asteroides Splendore, 1908, from Brazil, verrucous vegetations on the side and infected lymphatic glands.

S. jeanselmei Brumpt and Langeron, 1910, from a tumour on the knee. Shortly after operation the patient developed cutaneous and subcutaneous ulcerating gumma-like swellings, also involving glans and epidydimis. Periosteal nodes formed on tibia and ribs.

S. indicum Castellani and Chalmers, 1910, the cause of tropical sporotrichosis in Ceylon.

S. carougeaui Langeron, 1913, isolated from cutaneous ulcers in a tuberculous child in Madagascar.

S. fonsecai Pereira Filho, 1929, from nasal abscesses in a young girl in Rio Grande do Sul, Brazil.

Acremonium potroni Vuillemin, 1910. Not seen *in situ*, but cultures easily grown from pus; isolated from softening non-syphilitic gummatous nodules. The disease was ushered in with fever and intestinal symptoms. The subcutaneous nodules which were adherent to the skin formed later all over the body and were preceded by a violet discoloration of the overlying areas. Pulmonary, osseous and articular lesions have been referred to this species, also reported from a mycetoma of the ankle in Algeria.

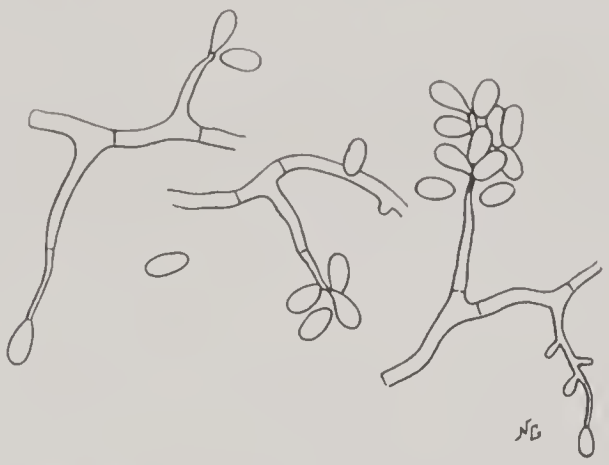

FIG. 53. *Acremonium potroni*. Cultural morphology. (Original)

Scopulariopsis blochi (Matruchot, 1911) Vuillemin, 1911, from a case of gummatous lymphangitis clinically resembling sporotrichosis.

Hormodendron algeriensis Montpellier and Catanei, 1927, from ulcerating chronic sporotrichoid lesions.

Mode of infection. De Beurmann and Gougerot discovered amongst fifty-seven white duvetous colonies of fungi found growing on various vegetables three of *Sporotrichum schencki*, thus demonstrating the fairly common existence of that species in nature. Together with this reservoir, the presence of the parasite in wild rats and in some domestic animals probably constitutes sources of infection to which man is exposed in rural areas and occupations and during his association with, or while handling diseased animals or their

carcases. Contagion, although recorded from man to man, appears to be a remote possibility.

The introduction presumably takes place by subcutaneous inoculation of the fungus carried on a traumatizing vegetable foreign body, by ingestion or by inhalation. Infection as a consequence of a rat-bite was reported by Lutz and Splendore in 1907, and by Moore and David (1918) from the bite of a mouse. Widal and Weill have succeeded in growing *S. schencki* from the blood in a case of generalized sporotrichosis, which goes far in explaining the reason why fresh lesions develop in patients who have not contracted new infections. It is interesting to note that it has also been isolated from the mouths of healthy individuals.

Morbid anatomy. There are no special features peculiar to this infection with regard to the changes it induces in the tissues. The usual reaction is similar to what is provoked by other chronic inflammatory processes like tuberculosis, actinomycosis, etc.

FIG. 54. Sporotrichosis. Lymphatic type. (After Magalhães)

Symptoms. The main characteristic of the disease is the production of sporotrichomas, gumma-like nodules of different sizes, as small as a pea or as large as an orange, in the skin or subcutaneous tissue of the extremities or trunk. This usually follows a slight injury, perhaps the prick of a thorn, which fails to heal. At first firm and painless, they tend to become tender and to soften in time, the overlying skin assumes a reddish or bluish hue with a slight central depression which breaks down into a fistula exuding a thin, serous or a thick, sero-purulent whitish or yellowish granular discharge. Healing may take place with irregular coarse scarring, or fully-developed ulcers with undermined bluish margins may form.

Deep-seated lesions have been found in muscles, subperiosteally, in joints, lungs, pharynx and larynx, epididymis, eye and other situations. This is the generalized type of infection, in contradistinction to the localized form in which swellings designated as

sporotrichic chancres are produced along the course of a lymphatic route draining the original lesion and are accompanied by lymphangitis. The general health usually remains unaffected and the lymphatic glands are not as a rule enlarged.

The majority of patients are adult males, but young children and old men are occasionally attacked. The disease runs a slow course, the lesions taking a long time to form and develop. Acute febrile septicaemic cases have been observed but may be regarded as exceptional.

Diagnosis. The parasite can sometimes be recognized in the lesions as yeast cells, free or incorporated by leucocytes, but, because of its scarcity in the pus, recourse should be had to growing it in culture form. De Beurmann and Gougerot recommend the following procedure for obtaining cultures of this species. It may be remarked that the steps suggested are, in essentials, natural precautions and are, or should be, followed on all occasions where cultures are attempted from pathological material.

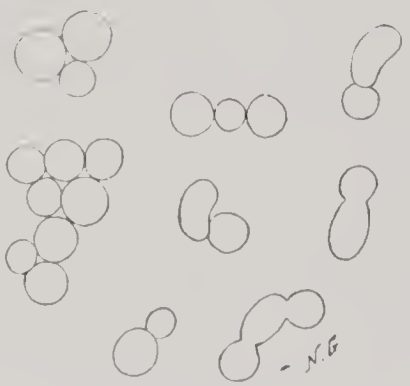

FIG. 55. Sporotrichosis. Budding yeast forms in pus. (Original)

Strict asepsis is enjoined in the operations. The pathological fluid is aspirated by means of a syringe from closed lesions or serum drawn by a pipette from ulcers or from under crusts after their removal. Sabouraud glucose-peptone medium is recommended and the material obtained is inseminated spread on three or four slopes in generous amounts, about 0·5 c.c. to each tube. The tubes are best allowed to incubate at ordinary room temperature away from the deleterious action of any laboratory antiseptic vapour like formalin, etc. For this fungus, the tubes are left unstoppered but well protected from dust. Colonies of fair sizes are obtained in about a week according to the general atmospheric temperature at the time. In the absence of culture media, the organism may grow on the surface of the glass if the pus is kept for a few days in dry sterile tubes.

Colonies are creamy, sometimes stellar, moist, shining, like a bacterial culture, turning more or less brownish or even black with age, becoming firmer and developing folds on the surface. Aerial hyphae may be seen as a slight duvet. Hyphae about 2μ in diameter, more or less branched, spores terminal, in rich masses or few in number along hyphae according to medium, pyriform, rarely on sterigmata, 1–2 × 0·5μ in size, becoming ovoid and brown in old cultures, 3–5 × 2–4μ. Optimum temperature, 22°–30° C.

According to de Beurmann and Gougerot, experimental inoculation of rats, who are especially susceptible to this infection, of pus from the lesions produces in the animals a generalized picture with a characteristic orchitis.

Because of its frequent association with, and the resemblance it bears to the cutaneous lesions of tuberculosis, this disease has to be excluded. Tertiary syphilitic manifestations, streptococcal lymphangitis, cold tuberculous or staphylococcal abscesses as well as similar mycotic infections with multiple abscesses, ulcers or nodules, such as other blastomycoses, actinomycosis, etc., are among the conditions for which it could be mistaken. Benign and malignant swellings are more possibilities to be taken into consideration in the differential diagnosis.

Treatment. Iodine offers the best hope for cure, which is often accomplished in a few weeks' time. Heavy doses of potassium iodide, 10 grammes in a litre of water, are to be taken daily unless idiosyncrasy contra-indicates its further use. To avoid iodism, other iodine preparations with which the market abounds can be administered, also in large doses. Local injections into the swellings —iodine 1 part and potassium iodide 10 parts in 500 c.c. of water, the same solution being used in dressing the open lesions—are beneficial and should be made simultaneously with internal iodine medication.

Hemisporosis

Definition. A mycotic infection similar to sporotrichosis inducing the production of indolent subcutaneous ulcerating gumma-like nodules, cold abscesses and osseous lesions.

Aetiology and history. The causative organism *Hemispora stellata* Vuillemin, 1906, was first reported from man in 1909 by Gougerot and Caraven in a case of osteoperiostitis, and de Beurmann, Clair and Gougerot, in the same year, isolated it from a gummatous tumour on the penis of a negro. In 1927 Fonseca and Arêa Leão found it again in sporotrichoid lesions on the arm, and Castellani *et al.* (1921) gave an account of a pulmonary infection to which they referred as broncho-hemisporosis. *H. stellata* invading the lungs was reported once more by Sartory in 1921 and by Perin in 1925, but it remains problematic whether this species acted in those instances as the true aetiological agent or was simply a superimposition on, or accidentally present with the tubercle bacillus as is probably the case in most of the so-called pulmonary mycoses.

H. stellata was originally isolated by Vuillemin in 1904 as a parasite on *Aspergillus repens* on some preserved fruit. It exists in nature as a saprophyte and is constantly occurring as a common laboratory contaminant. Its omnipresence is evidenced by its discovery by various authors in diverse and unexpected places. Bonjean (1898) found it in Paris water, and it was even recorded from the glacial heights of Mont Blanc. According to Tour, it has been isolated from the scales of a case of "pityriasis," probably an accidental inhabitant of the skin, as it provoked none of its typical lesions.

Mode of infection. It appears that by its general distribution the fungus is easily available for human infection, which seemingly

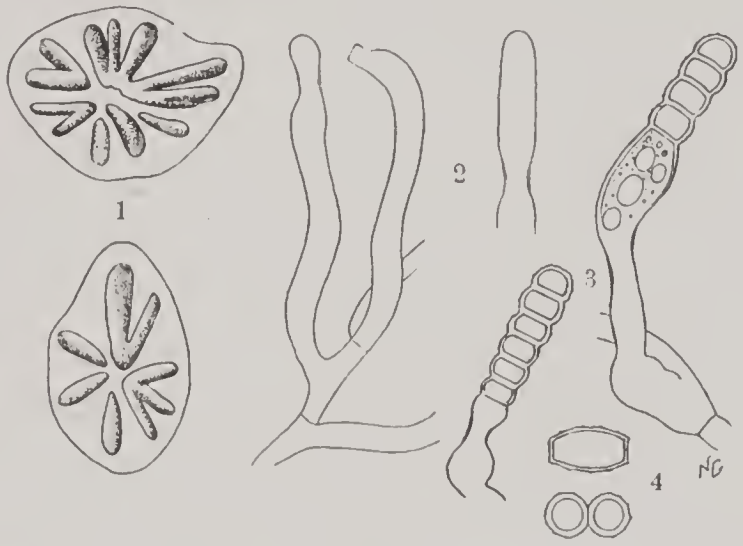

FIG. 56. *Hemispora stellata.* Cultural morphology. 1. characteristic stellar cultures, 2. protoconidia, 3. formation of deuteroconidia, 4. detached duetero-conidia. (After Vuillemin)

takes place through a breach of surface, external or internal, or by inoculation into the skin or mucous membrane.

Morbid anatomy. The nodules of hemisporosis present the usual appearances found in similar chronic inflammatory processes. There is a central softening part in which polymorphonuclear leucocytes and macrophage cells abound, surrounded by epithelioid and giant cells constituting a second zone which, in its turn, is enclosed in a third of markedly proliferating connective tissue. The osseous changes described are manifested as osteoperiostitis, hyperostosis and sometimes rarefaction.

Symptoms. In the cutaneous type of the disease, simple or multiple nodules simulating syphilitic gummata, tuberculous or sporotrichoid lesions, occur in various situations on the surface of the body, of which may be mentioned a cervico-facial localization, the tip of the

nose, the extremities, the abdominal wall, the gluteal region, etc. In time, the swellings soften and break down in the centre with resultant sinuses which may develop later into ulcers. Compared with similar tuberculous lesions, the suppurative process in hemisporosis is less pronounced, and the edges of the fistulous openings are softer, but the nodule itself is more markedly indurated.

In the case reported by Gougerot and Caraven, osteoperiostitis with hyperostosis of the tibia, suggesting tertiary syphilis, constituted the clinical picture. The same authors were successful in reproducing the osseous lesions experimentally in the rabbit by inoculation of the culture into the epiphysis of the animal's tibia.

The lesion reported from the penis on the corpus cavernosum was also mistaken for a syphilitic gumma, and showed marked central softening and rather exaggerated peripheral induration, both of which are typical features of the nodules in hemisporosis.

As for the occurrence of pulmonary hemisporosis with the attendant symptoms and signs of tuberculosis, it seems that the possibility should be accepted with reservations.

Cases of hemisporosis so far recorded include young adult subjects and one of a child of three.

Diagnosis. Cultures from material obtained aseptically from closed lesions for preference afford the best and practically the only means of arriving at a correct diagnosis. *H. stellata* has not yet been seen *in situ* except perhaps in a case of onychomycosis published by Falchi in 1925.

Colonies of *H. stellata* are white, 0·5–2·5 mm. in diameter, covered with conidiophores making little brown star-shaped spots. On sugar media, colony blackish brown, at first smooth and mamillate or irregular and coarsely convoluted, becoming powdered with ochraceous spores. Aerobic, not liquefying gelatin. Arthrospores in chains up to 30 or more, subspheric, 2·6–3·5μ in size with a fuliginous granular wall except on the facet of insertion, occasionally elongate and barrel-shaped. Hyphae 2–3μ in diameter, irregularly septate.

Treatment. Potassium iodide in progressively increasing doses is, as in sporotrichosis, very efficacious.

CHAPTER VII

BRONCHOMYCOSIS : OCULOMYCOSIS : OTOMYCOSIS : GENITO-URINARY MYCOSIS

Bronchomycosis

Without actually contesting the validity of mycotic infections of the lungs as true mycoses—at least not those of a secondary character—there are arguments that could be formulated against the absolute genuineness of primary implication. Some of the species incriminated in bronchomycosis, for instance those of the genus *Actinomyces*, exist unobtrusively as saprophytes in the body cavities, natural and otherwise, in the mouth, tonsillar crypts, carious teeth, and their elements may become included in the sputum on its way past these during expectoration. Particles of other species, available in the air, are liable to be continuously inhaled by everybody, apparently without producing serious deviations from the normal. Their incidence in the sputum seems to obey no rule other than that which governs their respective common occurrence or rarity at a given period in any particular locality. This is regardless of the presence or absence of tubercle bacilli or other factors in the patient. It may, therefore, be argued that the detection of mycelium, spores or yeast cells in the sputum or diseased lung tissue is scientifically no justification for diagnosing primary pneumomycosis. Moreover, most of the species in question fail to prove their pathogenicity on experimental inoculation. It would be more reasonable to accept bronchomycosis only as a complication coincidental with, or superimposed upon, some pulmonary devitalization of a bacterial or other character.

Aetiology. There is a rich variety of species of fungi that has been isolated from expectorations, open lesions on the parietes of the chest communicating with its cavity and from lung lesions in the *post-mortem* room. The cultures obtained from such material represent all groups of fungi connected with man; but an outstanding feature about them is the comparative infrequency of their recurrence from similar cases labelled as bronchomycosis. The more

common species are *Aspergillus fumigatus* Fresenius, 1850, as well as other members of the family *Aspergillaceae*, all of which are ubiquitous saprophytes. Next in order of frequency are the yeasts and yeast-like species. The genus *Actinomyces*, although encountered less often, accounts for a fair number of cases, while others yield a few species of *Penicillium* and *Alternaria sp.*, and pulmonary hemisporosis and sporotrichosis are also on record. Of the *Mucorales*, *Absidia corymbifera* (Cohn, 1884) Saccardo and Trotter, 1912, *Rhizopus parasiticus* (Lucet and Constantin, 1900) Lendner, 1908, *R. niger* (Ciaglinski and Hewelke, 1893) Barthelat, 1903, and *Mucor racemosus* Fresenius, 1850, are amongst the early species that started the institution of bronchomycosis as a clinical entity.

Healthy tissue in healthy individuals can easily be pronounced as sufficiently resistant to combat infection in most cases in the absence of predisposition. Any state tending to lower the organism's body or bronchial tone, such as industrial pulmonary diseases, trauma, the common infections, heredity and, probably to a very great extent, tuberculosis, will operate as an important factor in favour of pneumomycosis. Under such circumstances, the introduction of fungus elements into the bronchioles will aggravate a concomitant or antecedent morbid state. The implanted organism will thrive in a medium made suitable for its reception and, acting as a foreign body, can cause by mechanical irritation as well as by its metabolic products and toxins, general and local interference with the proper functioning of the tissues involved.

The incidence of bronchomycosis is highest among farm-hands by virtue of their association with bovidae, plants and the soil, the former being sources of parasitic species, while the two latter are rich in saprophytic elements. Infection is more prevalent in males who are naturally more exposed than females, while for the same reason, children are rarely affected.

Morbid anatomy. Nodule formation on the same lines as in a tubercular process occurs in some cases. Their dissemination is variable and may be miliary. Suppuration, haemorrhage, necrosis and caseation are followed by cavitation, which evolution induces the usual zones of tissue and cellular reactions around the focus of infection. Islets of bronchopneumonia and progressive sclerosis of pulmonary tissue, interspersed by necrotic cavities, and vascular thrombosis are the morbid features in advanced cases. Fungus elements may be demonstrated in the alveoli, bronchioles, the walls of the blood-vessels or the cavities. Evidence of primary actino-

mycotic infection in the mediastinum leading to secondary invasion of the lungs or thoracic wall may be present. As bacterial infection in most cases is actually the dominant factor in the production of pathological changes, these will only be slightly modified by the presence of the fungus.

Symptoms. There is no pathognomonic syndrome by which a given case could be recognized as bronchomycosis. Suspicion is sometimes entertained when it is a question of a chronic pulmonary condition which by its symptoms and physical signs suggests a tuberculous infection and, at the same time, granules, yeast cells, mycelium or spores are demonstrated in the sputum, with or without the *Mycobacterium tuberculosis*. Failure to find tubercle bacilli, however, has no positive value; they may be absent from one day's expectoration, only to reappear on a subsequent day, or else, because there is no uniformity in their distribution, different smears from one specimen yield opposite results.

There are cases of simple chronic cough or asthmatic attacks that represent no more than simple deposition by inhalation of mycelial elements in the bronchi; and, provided that no previous damage to tissue has occurred, the signs and symptoms will be mainly those of mechanical irritation or allergic reaction producing slight cough with mucous expectoration and a few râles and rhonchi, and the condition may be clinically diagnosed as chronic bronchitis or asthma. On examination of the sputum, mycelium is occasionally discovered, and the case is promptly labelled as bronchomycosis. Without hair-splitting, it may be granted that distinction and the patient is found to respond well to potassium iodide medication.

In illustration of inhalation mycoses where the individual is more or less constantly exposed to an atmosphere laden with gross or microscopic particles of foreign matter in which, presumably, fungus elements are included, examples of more severe forms may be cited. This refers to some occupational lung affections which are considered as bronchomycoses. There is the well-known "tea-taster's cough" which is met with in parts where tea is grown in large quantities. A tea-taster, besides tasting brews of tea for grading and blending purposes, has to rely as well on his olfactory sense by sniffing up from handfuls of tea leaves into which he buries his nose, thereby inhaling quantities of tea-dust. This has been found by Castellani (1906) to contain blastospores and *Aspergillus* and *Penicillium* spores.

The same type of cough is also complained of by the coolies in tea factories where again the air is rich in tea-dust. A chronic cough and

mucous or muco-purulent sputum with a few râles over the chest are the first symptoms and signs followed by loss of weight and general weakness. If a different open-air occupation is assigned to the worker who develops these symptoms, he eventually recovers. Castellani discovered yeast cells in these patients' expectorations, but how far these affections are referable to the effect of inhaled fungi or to the tea-dust as such acting in the same manner as coal-

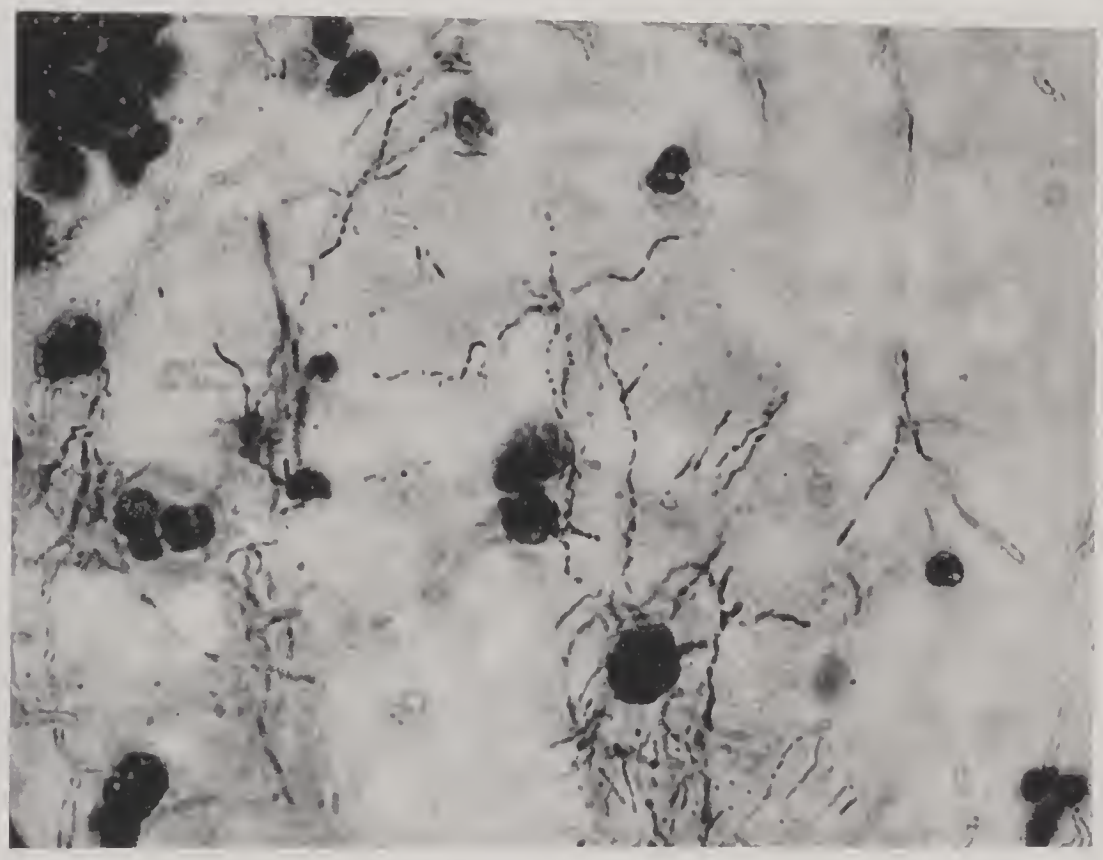

FIG. 57. Filaments of *Actinomyces albus* in sputum. (Original)

dust affects miners or as similar foreign matter in industrial centres causes silicosis, siderosis, etc., is rather debatable.

Another occupational "bronchomycosis" occurs among breeders of birds, and is ascribed to the practice of artificially feeding the newly hatched birds, especially pigeons. The breeder fills his mouth with dry grains of maize or beans which he forcibly blows through the beak, held between his lips, down to the crop. Hair-combers who powder the hair with rye flour which is rich in spores of *Aspergillus* are also subject to yet another type of occupational "bronchomycosis." The pulmonary affections in these cases, like the tea-taster's cough, are liable to develop into fibrosis of the lungs and may go on later to phthisis.

In the presence of bacterial lung disease the clinical picture and signs are of a more complicated nature, and all degrees are encountered, from a mild form to states which may be regarded by their respective signs and symptoms as pleurisy, bronchiectasis, pneumonia, bronchopneumonia, pulmonary gangrene, tuberculosis, etc. The resemblance to phthisis is generally seen in actinomycotic or blastomycotic infections, as in *Coccidoides immitis* and *Paracoccidioides brasilieusis* primary lung invasion. Pyrexia, night sweats, cough with haemoptysis, dyspnoea, thoracic pain and emaciation constitute the usual symptoms, and the *Mycobacterium tuberculosis*, granules, or other mycelial elements may, as often as not, be found in the sputum. Restriction of the infection to the lung may eventually be broken down, the pleura and chest parietes may become involved, and abscesses, sinuses and fistulae result. There can be little doubt that these complications are less likely to arise without the added agency of the fungus to the original bacterial invasion. The physical signs naturally vary with the different stages in the progress of the disease and with the extent of tissue destruction. Contrary to what takes place in phthisis, the apices usually remain free in bronchomycosis of actinomycotic or blastomycotic aetiology, while the right lung is more commonly affected than the left.

FIG. 58. *Aspergillus fumigatus*. Growth on Sabouraud 2 per cent glucose-agar. (Original)

When the lung is implicated through extension from elsewhere of some mycotic infection, the appearance of pulmonary symptoms and signs where none previously existed may supply evidence of the new complication. For lung involvement by contiguity, actinomycosis of the oesophagus is an example. Histoplasmosis of Darling, sporotrichosis, Gilchrist's or other generalized blastomycosis

and hemisporosis may eventually attain the lungs among other organs.

Diagnosis. One method of diagnosis is the discovery of mycelium, spores, yeast cells, granules or fine bacilliform filaments of *Actinomyces* in the sputum. The commonest elements discoverable are in the order of incidence, yeast cells, filaments of *Actinomyces*, spores,

FIG. 59. *A. fumigatus.* Stalk and head bearing phialides and some undisturbed conidial chains. (Original)

and, rarely, heads of *Aspergillus fumigatus*. When none of these is demonstrable, cultures, more often than not, yield growths of various species, but these are often discovered to be mostly saprophytes that might just as well have been obtained from apparently normal persons. Reliance on microscopic examination of the sputum is of practical importance, as the detection in it of fungus elements is strong evidence of their abundance, and therefore of their deleterious effect on the lungs and probable agency in the production of the disease. Specific diagnosis, however, is arrived at through careful consideration of microscopic evidence as well as cultural results without neglecting case-history, occupation, together with antecedent or concomitant significant infection.

Colonies of *A. fumigatus*: velvety or felted, spreading, dark green becoming almost black with age, optimum temperature 37° C. Mycelium

septate or non-septate, greenish, greyish or almost black, 2–3μ in diameter. Conidiophores 300 × 2–8μ in size, borne on submerged or aerial hyphae ending in flask-shaped vesicles 20–30μ in diameter. Primary phialides on the vesicles 5–10 × 2–3μ, usually only covering the top half of the vesicle. Each carries dark green or colourless, spherical, rarely ovoid, smooth chains of conidia, 2–3·5μ in diameter.

Treatment. Potassium iodide or other iodine preparations in large doses continued over long periods offer the only available therapeutic measures in pneumomycosis. Many cases respond promptly and are finally cured. General hygienic measures on the same lines followed in the treatment of phthisis are also advisable.

Oculomycosis

This subject, like most mycoses, is based on isolated cases possessing features which hardly serve to distinguish them from other affections of the eye. It is here presented in a restricted form, as a more comprehensive account is neither necessary nor within the scope of this work. For all practical purposes, the first aim is to draw attention to the various possibilities of fungi in connection with the eye, secondly to diagnose them as such, which result is only achieved through the detection of fungus elements in the lesions, as well as their cultural individualities, and lastly to attempt cure by ophthalmological local or surgical measures, together with the unique drug, potassium iodide. The lesions are enumerated in relation to their sites, and to avoid repetition, detailed descriptions of their characters are omitted as they are available on reference to the general accounts of the respective mycoses.

Various species of fungi have been isolated or presumed from lesions of the eye and its adnexa. In the majority of cases, they represent either extension by contiguity of a mycotic affection or else a manifestation of a generalized mycosis. Traumatizing foreign bodies, such as particles of stone, metal, coal, straw, etc., presumably carrying fungus elements, play an important rôle in their introduction into the eye and probably in the institution of a true mycotic lesion. Innocuous saprophytes and even pathogenic species have been found to inhabit seemingly normal eyes, but in the presence of bacterial infection, or following upon trauma, they have been known to produce complicating lesions of a superficial and benign nature in some cases or more damaging results in others.

Most of the organisms isolated from cases of oculomycosis have either not been tested for their pathogenicity or else proved

non-pathogenic to the rabbit's or the dog's eyes. Some of them are set down below as a demonstration of their variety.

Species of *Actinomyces* have mostly been found in corneal lesions, in cases of conjunctivitis, and in concretions in the lacrimal canal, while isolated ones have been recovered from the eyelids and from cases of irido-cyclitis. Some of these species are:

Actinomyces föresteri (Cohn, 1874) Gasperini, 1894, in concretions in the inferior lacrimal canal.
A. albus (Rossi-Doria, 1891) Gasperini, 1896, in conjunctivitis and dacrocystitis.
A. carneus (Rossi-Doria, 1891) Gasperini, 1894, in conjunctivitis and dacrocystitis.
A. aureus (DuBois, Saint-Severin, 1895) Lachner-Sandoval, 1898, in conjunctivitis and in the caruncula lacrimalis.

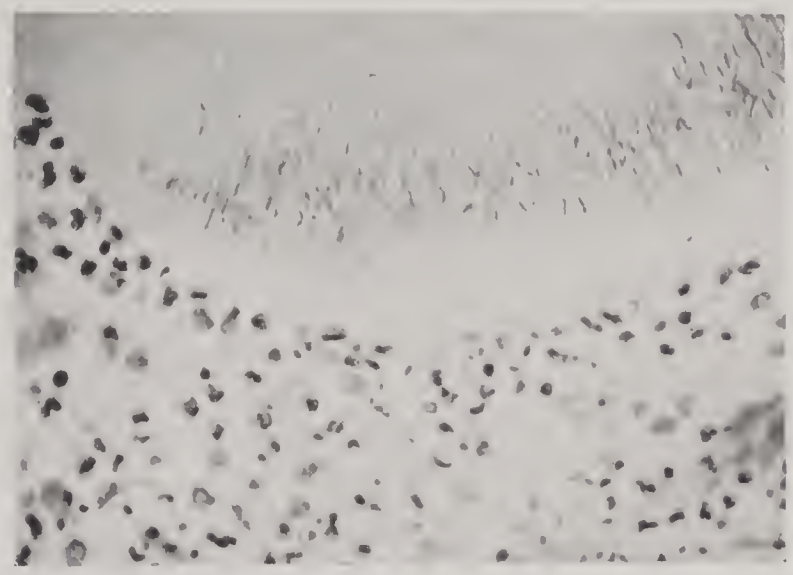

FIG. 60. Part of the circumference of a grain of *Actinomyces dassonvillei* from an orbital tumour. Note the peripheral mycelium and the surrounding tissue reaction. (Original)

A. luteolus (Foulerton and Jones, 1902) Brumpt, 1927, in conjunctivitis.
A. cerebriformis Namyslowski, 1909, in the cornea.
A. radiatus Namysłowski, 1909, in the cornea.
A. dassonvillei (Liégard and Landrieu, 1911) Brumpt, 1927, in conjunctivitis.
A. zur-neddemi Namysłowski, 1912, in the eyelid and the lacrimal duct.
A. de berardinis Namyslowski, 1912, in conjunctivitis, and has produced corneal ulcers by accident.
A. roseus Namyslowski, 1912, in the cornea.
A. purpureus Cavara, 1912, in the cornea.
A. discofoliatus Gruter, 1933, in concretions in the lacrimal canal.

Of the *Mucorales*, Aspergilli and Penicillia, the following species have been isolated mostly from the cornea and conjunctiva:

Absidia corymbifera (Cohn, 1884) Saccardo and Trotter, 1912.
A. cornealis (Cavara and Saccardo, 1913) Dodge, 1935.

Aspergillus flavus Link, 1809.
A. fumigatus Fresenius, 1850.
A. niger, Tieghem, 1867.
A. flavescens Wreden, 1867. (Not cultivated.)
Scopulariopsis koningi (Oudemans, 1902) Vuillemin, 1911.
Penicillium crustaceum (Linné, 1753) Fries, 1832.

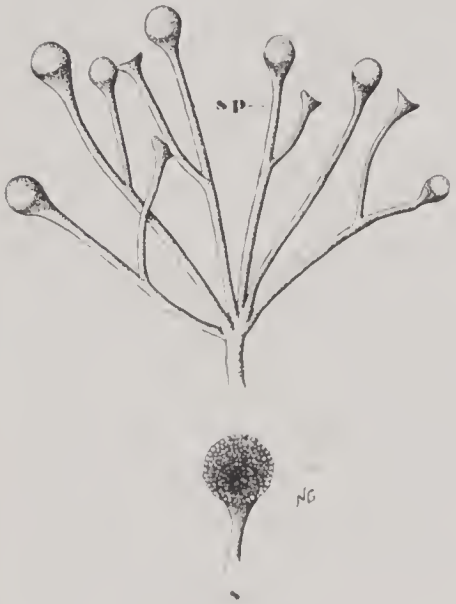

FIG. 61. *Absidia cornealis*. Cultural morphology. Ramifications in umbels. sp. sporangiophore, s. mature sporangium. (Original)

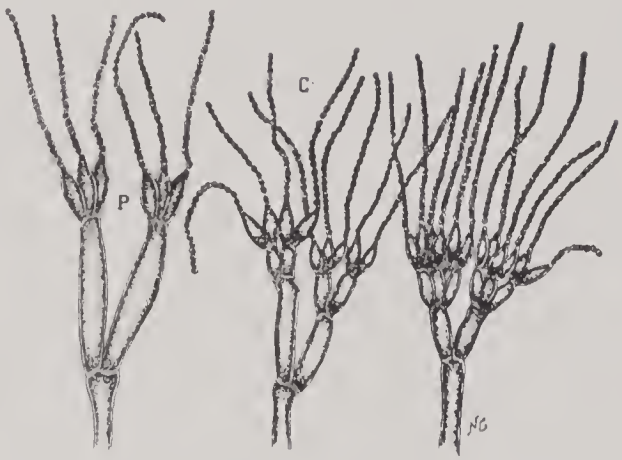

FIG. 62. *Penicillium crustaceum*. Cultural morphology. P. phialides, C. conidia. (Original)

In generalized sporotrichosis, lesions of the eye are caused by:

Sporotrichum schencki (Hektoen and Perkins, 1900) Matruchot, 1910.
S. jeanselmei Brumpt and Langeron, 1910.

Other *Sporotricheae* reported from the eye are:

Trichosporium graphii (Harz and Bezold, 1889) Dodge, 1935, from the cornea.
T. gammeli (Pollacci and Nannizzi, 1927) Dodge, 1935, from the cornea.

Foci in the eye have occurred in generalized blastomycosis due to:

Coccidioides immitis Stiles, 1896.
Zymonema dermatitidis (Gilchrist and Stokes, 1898) Dodge, 1935.

Exceptionally, ocular lesions have been recorded as caused by:

Rhinosporidium seeberi (Wernicke, 1900) Seeber, 1912.

Among species of yeasts and yeast-like fungi occurring mostly in corneal lesions are:

Castellania tropicalis (Castellani, 1910) Dodge, 1935. (= *Monilia tropicalis*).
Syringospora albicans (Robin, 1853) Dodge, 1935. (= *Monilia albicans*).
S. cavarae (Pollacci and Turconi, 1928) Dodge, 1935.

Proteomyces cornealis (Nannizzi, 1929) Dodge, 1935.
Debaryomyces lundsgaardi Ota, 1923.

Miscellaneous species include:

Pullularia pullulans (Bary, 1868) Berkhout, 1923, in conjunctivitis.
Spicaria rubra (Baquis, 1905) Dodge, 1935, in keratomycosis.
Cephalosporium serrae Maffei, 1930, in keratomycosis.
Beauveria brumpti Langeron and Lichaa, 1934, in conjunctivitis and keratitis.

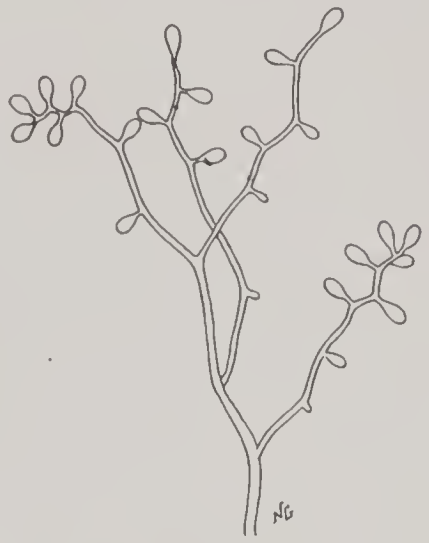

FIG. 63. *Beauveria brumpti.* Cultural morphology. (Original)

The Eyelids, Eyebrows, Eyelashes and Ciliary Margins

Actinomycosis, sporotrichosis and blastomycosis, including coccidioidal infection and Gilchrist's dermatitis, may secondarily, or rarely primarily, attack the skin of the eyelids and orbital border or the palpebral margins.

Actinomycotic infection is usually by extension from neighbouring lesions on the face, and may go on to osteoperiostitis with discharging sinuses and fistulae. In sporotrichosis, multiple, hard, dermohypodermic nodules are formed; they become violet in colour, soften, break down and finally ulcerate. Adenopathy of the submaxillary and pre-auricular glands is a common accompaniment. When the ciliary margin is affected, circumscribed folliculitis and multiple ulcers result. Assuming an irregular outline, some may become encrusted and ectropion may occur, either from the sporotrichic lesion, or because of secondary infection and swelling of the palpebral conjunctiva. Miliary subcutaneous abscesses, isolated or confluent nodules, or vegetant lesions constitute the various pictures

noted in the different types of generalized blastomycosis. In these cases the conjunctiva is as a rule spared.

Trichophytic, microsporic and favic lesions are occasionally met with on the glabrous skin of the lids and orbital border, but the infection is generally arrested short of the eyebrows and eyelashes. When the latter are involved—a rare occurrence—there is an accompanying blepharitis. The lesions are invariably secondary to infection in the vicinity or elsewhere, especially on the scalp.

Species of *Mucorales*, *Aspergillus*, *Penicillium* and allied organisms have been isolated from the eyebrows on rare occasions and constitute mere saprophytic deposits, although chronic scaling with pruritis is sometimes produced without involvement of the hairs.

The Lacrimal Apparatus

Actinomycosis of the lacrimal apparatus is more commonly found in the canal, and it is only rarely that implication of the gland, sac or naso-lacrimal duct takes place by extension from it. The incidence constitutes a very small percentage of lacrimal affections and varies with the locality. Females are more often affected than males, and practically no age is immune. As a rule secondary to actinomycosis elsewhere, it may also occur in association with non-mycotic pathological states in the eye. Next in the order of incidence, sporotrichosis and rhinosporidiosis have been reported as causing dacrocystitis, while the gland, or indeed any part of the tear organs, may become involved in endocular or orbital actinomycosis. Apart from its occasional presence and accidental discovery in the tears, *Aspergillus* filaments have been found to occlude the lacrimal canal more or less completely.

In actinomycosis of the lacrimal duct masses of filaments or granules may form and are often mixed with calcareous deposits. These concretions may be single or multiple, of different sizes and colours, and tend to affect the patency of the passage with the usual attendant symptoms. A painless circumscribed swelling is seen over the duct, and an angular or palpebral conjunctivitis, probably with pruritis, lacrimation, tumefaction of the ciliary border corresponding to the affected canal and dilatation of the *punctum lacrimale* are the main signs and symptoms. From the punctum a bead of viscid, purulent discharge can be expressed and examined for diagnostic purposes.

Suppurative dacrocystitis of sporotrichic aetiology has been

reported with enlargement of the pre-auricular gland, and is either primarily cutaneous involving the sac secondarily, or vice versa.

Elements of *Rhinosporidium seeberi* have been found in the lacrimal sac among the other aberrant sites of this species. There are probably more instances than is suspected which occur by extension from the nose to the naso-lacrimal duct and sac.

The Conjunctiva

It is possible for species of *Actinomyces*, *Mucorales*, *Aspergillaceae*, etc., to exist saprophytically on normal or diseased conjunctivae, and when they institute a morbid process, this is generally favoured by concomitant bacterial infection or trauma.

Fig. 64. Nodular actinomycosis of the conjunctiva. Case of *Actinomyces aureus* infection. (Original)

Actinomycosis of the conjunctiva may assume one of two forms. A diffuse lesion, resembling catarrhal conjunctivitis, with its usual attendant signs and symptoms, is described. It is as a rule unilateral, of chronic duration, and it fails to respond to the common attempts at treatment. The second type is of a nodular character, favouring the bulbar conjunctiva for a site, and resembles lesions due to tuberculous infection. The palpebral conjunctiva may similarly be affected, and the nodules are apt to be confounded with those of sporotrichosis or tuberculosis.

In generalized blastomycotic infections the conjunctiva usually escapes, except for some secondary inflammation, sometimes with ectropion, co-existent with blastomycosis of other parts of the eye. Pterygium is also on record.

Sporotrichosis, in the course of a disseminated infection, affects the conjunctiva in the form of gummatous, hard, painless nodules of various sizes, or as granulating ulcers. The latter occur when the palpebral part is implicated, and are of sizes varying from 1 to 3mm. Reddish-blue in colour and slightly elevated, they give the membrane a strawberry-like aspect. General congestion is a regular

accompaniment. The lesions are difficult to diagnose clinically as they often simulate those of tuberculosis but respond to potassium iodide medication.

The bulbar conjunctiva has been reported as an exceptional site of *Rhinosporidium seeberi* infection. The lesion produced is in the shape of a granuloma the size of a lentil, of a pinkish colour dotted with greyish points and with distended vessels radiating from it. A case reported was of three years' duration, and the tumour recurred after excision.

Species of *Mucorales* only occur in the conjunctiva as saprophytes, probably in association with catarrhal or more severe types of conjunctivitis without contributing to the morbid process.

Aspergilli may be part of the presumably normal fauna and flora of the conjunctiva and are mentioned as a complication in connection with aspergillar keratitis or corneal ulcers. In some instances, the fungus, apart from attacking the cornea, may produce alterations in the conjunctiva. Engorgement and irregular swelling with papillary excrescences constitute one form of change which occurs in the bulbar part. In other cases, the palpebral portion is congested and covered by a fine, greyish or yellowish, slightly adherent membrane, either alone or overlying a superficial ulceration.

Likewise, *Penicillium* and other species may, as saprophytes, form part of the conjunctival organisms in apparently normal eyes or in the course of bacterial infection. Greyish-green patches composed of epithelial conjunctival cells, polymorphonuclear leucocytes, mucus and fibrin, may be formed on the bulbar or palpebral conjunctiva as a result of *Penicillium* implantation.

The Sclera

Being inert, the scleral tissue is little liable to infection in general. Its involvement in mycosis is also of rare occurrence and is usually consequent upon lesions elsewhere in the eye. Sporotrichosis, and less commonly aspergillosis, are recorded. In particular, the superficial episclera may be the site of sporotrichomas in the course of disseminated sporotrichosis. The nodules are about 1 mm. in diameter, yellowish in colour, and the overlying conjunctiva shows distended vessels. When softened, pus may be aspirated, and colonies of *Sprotrichum* grown from them. On the other hand, the original infection may be situated in the ciliary body and extends thence by perforation to the deep part of the sclera. Aspergillosis

may produce whitish or yellowish-white, small, fleshy or hard, granulomatous tumours of the episclera.

The Cornea

Corneal ulcers, occasionally with hypopyon, may be due to implantation of species of *Actinomyces* which seem to invade the cornea more than the rest of the eye. The features of the lesions are not, however, sufficiently diagnostic from a clinical point of view. Actinomycotic ulcers are usually superficial and have a tendency to peripheral rather than deep spread with infiltrated and excavated borders. They vary in number, situation, size and colour, assuming yellowish or greyish hues, and in the case reported as due to *Actinomyces purpureus*, the ulcer was purplish in colour. Complicating hypopyon may sometimes occur. Instead of ulceration, actinomycosis of the cornea may induce the formation of tiny nodules, sometimes granulating, 1–2 mm. in diameter, with sharp edges and slightly raised above the surrounding normal tissue. They vary in colour between shades of white, yellow and red to brown. Conjunctival reaction is often present, or a band of dilated vessels may be seen coursing from the limbus to the lesion.

All stages of corneal lesions, from simple keratitis, a membranous layer or tiny protuberances to ulcer formation and hypopyon, have yielded species of yeasts and yeast-like organisms. They are, as a rule, secondary to palpebral or generalized blastomycosis or else complicating non-mycotic affections of the eye.

In disseminated sporotrichosis, corneal gummata or ulcerations may be produced, sometimes alone but more often following sporotrichic conjunctivitis or irido-cyclitis.

Keratomycosis of aspergillar origin is the commonest of ocular mycoses, and manifests itself as nodular or, more often, as ulcerative lesions, in some cases with hypopyon. The ulcers are discoid, whitish or yellowish, rather dry, and surrounded by a ring of infiltration. The nodular lesions are indistinguishable from those due to other types of mycotic infection in the eye. They appear as white, opaque, dry, irregular small swellings with a band of distended vessels running towards them from the direction of the limbus, while occasionally they are surrounded by a congested ring. Fascicular keratitis is the nearest approach in its characters to nodular aspergillosis of the cornea, except for the slower evolution of the latter.

Of much rarer incidence is keratomycosis due to species of *Penicillium* or *Mucor*. The lesion in a case of a mucorine infection was a small double nodule, opaque white, with vessels proceeding to it from the limbus, and lacking the ring of demarcation or the infiltration occurring in similar lesions of aspergillar aetiology. This case was complicated with hypopyon and iritis. Keratitis due to *Aspergillus*, *Penicillium* and similar species is recorded in which the main feature is superficial ulceration with distended vessels converging towards the corneal focus.

Intra-Ocular Mycosis

During deep operative interventions on the eye, or following upon trauma, species of *Actinomyces*, yeasts, *Aspergillus*, etc., may gain access into the eyeball and cause intra-ocular lesions. Actinomycotic involvement, of which little is recorded, and that mainly at autopsy or after enucleation, especially affects the chorioid and ciliary body. Nodules on the retina, the episclera and irido-cyclitis are recorded. In cases of actinomycosis of the orbit, secondary to lesions elsewhere, the bulb may suffer in varying degrees and situations up to panophthalmitis.

Sporotrichic iritis, irido-cyclitis and retinitis are all possible in connection with disseminated sporotrichosis with the formation of sporotrichomas on any of these parts.

Secondary to aspergillar keratitis or ulcer or after trauma, an exudative inflammation of the anterior chamber may take place, and panophthalmia sometimes ensues.

Diagnosis and treatment. The lack of pathognomonic features about ocular mycoses emphasizes the importance of the necessity to have recourse to microscopic examination, biopsy and culture of pathological material. As far as treatment is concerned, the usual ophthalmological curative methods are applicable with the addition of potassium iodide orally, or some iodine preparation by the intramuscular route.

Otomycosis

Although distinguished as a mycosis, this condition is no more or less than an occasional accidental implantation and multiplication of a saprophytic fungus in the external auditory meatus. The species isolated from catarrhal or suppurative discharges of the middle ear are also in the nature of air-borne contaminants.

Aetiology. It can safely be maintained that otomycosis is always secondary to infection or trauma of the external auditory canal. Fungus elements are liable at times to be deposited there, but unless a favourable substratum for their growth is available in the form of a breach of surface with moisture and exudate or excessive neglected cerumen, they can gain no foothold. As in some other affections of the ear, the bathing season is a particularly favourite time for trouble to start. The continuously moistened wax causes irritation which sometimes leads to attempts on the part of the patient for its removal to relieve the symptoms. Oils, cotton-wool plugs, wooden applicators, etc., usually none too clean, are employed rather indiscriminately and carelessly; injury to the epidermis of the meatus or even the tympanum may be inflicted, and we have the requisites for any wandering species to thrive if accidentally introduced.

FIG. 65. *Rhizomucor septatus.* Cultural morphology. (After Siebenmann)

The species reported as causing otomycosis are mostly members of the *Aspergilliaceae*, of which *Aspergillus fumigatus* Fresenius, 1850, is an often recurring representative. Of the *Mucorales*, *Mucor pusillus* Lindt, 1886, as well as *A. siebenmanni* Lucet and Constantin, 1905 (=*A. flavus* Siebenmann, 1883), *A. niger* Tieghem, 1867, and *A. malignus* (Lindt, 1889) Thom and Church, 1926, *Rhizomucor septatus* (Bezold, 1889) Lucet and Constantin, 1901, *Absidia corymbifera* (Cohn, 1884) Saccardo and Trotter, 1912, and *A. ramosa* (Lindt, 1886) Lendner, 1908, have been found. The latter species, it is interesting to note, has been isolated from the nasal secretions of the horse, and Castellani reports the organism from two cases of otomycosis occurring in horse-keepers. One or two yeasts are also encountered. The ear itself can equally well be the site of the usual mycotic lesions that might affect the skin elsewhere. Rhinosporidiosis and actinomycotic infections are also possible. Young adult males are more commonly affected than females or children, especially in rural surroundings.

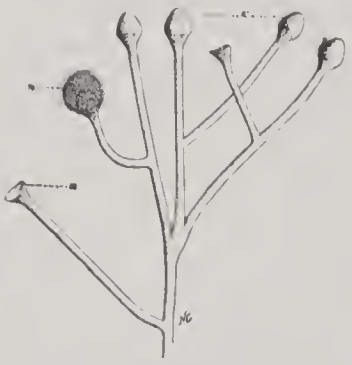

FIG. 66. *Absidia corymbifera.* Cultural morphology. Corymbiform ramifications. a. funnel-shaped apophysis, s. sporangium, c. columella after dehiscence of sporangium. (Original)

Symptoms. The common symptoms are those of local irritation due to the presence of a foreign body in the external auditory canal unless middle-ear disease also exists, in which case its symptoms are additional features. Generally speaking, a sense of fullness, *tinnitus aurium*, itching, impaired hearing, and pain, especially at night, are complained of in varying degrees. Reflex effects from pressure on or damage to the tympanic membrane may occur with more or less complete deafness, vertigo and cough.

On examination, the canal is found to be occluded by a cottony plug of a black, white, brown, yellow or green tint representing the respective coloration of the particular fungus mixed with cerumen, dirt, discharge, more or less modifying its original colour, and sometimes strands of cotton wool, the remains of a plug used by the patient himself. A whole plug of wool, totally forgotten, is sometimes discovered. On removal, the mass may be teased and its nature verified under the microscope or by culture as a matter of interest. Behind it the walls of the meatus and the tympanum may be hyperaemic, raw or bleeding with perhaps scattered spots of still adherent mycelium. The tympanic membrane may be perforated.

Treatment. Attempt is carefully made to remove the mass with forceps, piecemeal or as a whole if practicable. Failing this, it may be softened by instillation of carbolic, glycerin and sodium bicarbonate drops and then syringed out with a warm antiseptic solution. The wash may have to be repeated to ensure total removal of the fungus, and in any case to avoid relapse. Hydrogen peroxide solution, or 1 in 2,000 potassium permanganate are useful for that purpose.

Genito-Urinary Mycosis
" Vaginal Mycosis "

A healthy vagina may be regarded as unlikely to harbour fungi, but a few might exist as saprophytes without their presence being suspected. Abnormal vaginal conditions have been an urge to pathologists to inoculate discharges on artificial media, and they yielded mainly yeasts and yeast-like species, including those of thrush —less commonly *Actinomyces*, *Hemispora*, Aspergilli, Penicillia and other saprophytes whose pathogenicity is more than doubtful and which probably occur in healthy vaginal secretions. The majority of these organisms have been diagnosed without culture and their generic nature only roughly ascertained from their characters in the pathological material under the microscope.

The subject of mycotic infection of the vagina owes its origin to cultural results in cases of vaginitis, vulvo-vaginitis and cervicitis, where discharge is the main complaint. Whether this is primarily due to the fungi isolated, or else that these are co-existent with or superimposed upon a previous bacterial infection, of which gonorrhoea may be cited, is a debatable point. Denuded or devitalized surfaces, however, are quite receptive to deposits of fungus elements. The discharge, and in some cases the soiling in the vaginal vicinity by diabetic urine, offer favourable media for the growth of the species obtained and incriminated as aetiological agents.

The usual loose, whitish, leucorrhoeal discharge is the most common complaint, but it may be viscous, muco-purulent or even frankly purulent according to the nature of the bacterial lesion present. Though rare, black and red varieties are reported, the abnormal coloration of the discharge being ascribed by Castellani to a red pigment-producing *Cryptococcus*, while the darker hues are due to *Aspergillus*, *Penicillium* and other filamentous saprophytes. Some of the above-mentioned species have also been recovered from the vulva and ano-perineal regions, either alone or in association with *Epidermophyton*. Apart from the discharge, burning of varying intensity, soreness and probably a certain amount of pruritis may be induced.

The lesions encountered range from cervicitis and erosions to vaginitis with white spots or patches and vulvitis in the form of circumscribed areas involving the labia alone or extending more or less widely over the neighbouring parts. Spread of the infection may in some cases implicate the urethral opening. Perineal and vulvo-vaginal lesions in which elements of fungi have been demonstrated occur as a general rule amongst suckling infants in whom the mycosis may be in reality an added factor to a primary napkin dermatitis, especially in the poorer classes.

Diagnosis. Culture may yield some fungus species which, however, should not be taken too seriously or preclude further search for a primary underlying bacterial or other explanation for the lesions.

Treatment. Irrigation with alkalis alternating with antiseptic lotions may be tried. Weak iodine or potassium permanganate solutions are recommended, and in some instances creosote, 20 grammes in olive oil, 60 grammes, has brought about a cure.

Blastomycosis of the Female Reproductive Tract

Hamblen *et al.* (1935) reported a case of blastomycotic infection of the endometrium, myometrium and Fallopian tubes by *Zymomema dermatitidis* (=*Blastomyces dermatitidis*) the aetiologic agent of Gilchrist's disease, or American blastomycosis, a clinical rarity in the female reproductive organs. The woman, aged 27, suffered from blastomycosis of the lungs, and developed menorrhagia, irregular menses, and a serosanguineous vaginal discharge. Two masses about 3–3½ in. in diameter, tender and firm, were felt on either side of an apparently normal uterus. Curetted endometrium and endocervix revealed double-walled budding yeast cells on section. The uterus, right tube, left tube and ovary were removed by operation. These organs were involved in peritoneal adhesions to some of the pelvic viscera. Tubercles with giant cells, often incorporating blastomycetes, were especially numerous in the wall of the tube and also along the uterine cavity and in the peritoneum. Miliary abscesses with thick fibrous walls in the uterine wall and tubes were found. Pus was present in the proximal end of the tube and in pockets on the posterior surface of the broad ligament. Necrotic changes were evident at a point along the tube, probably in relation to abscess pockets.

Fungi Isolated from the Urinary Tract

Actinomyces and *Aspergillus* have been obtained from renal infections, cases of pyelonephritis and after nephrotomy, but the value of these findings as evidence of true renal mycosis is doubtful in view of possible contamination. From the urine, in some cases aseptically withdrawn, yeasts and yeast-like species as well as *Aspergillus* have been grown; but the factor of contamination, in the majority of cases, cannot be totally overlooked. Diabetic urine has also yielded growths, and generalized mycosis may involve the bladder.

Discharge from the urethra has been found to contain species of fungi in cases known to be of acute or of chronic gonorrhoea, as well as in instances where such history or positive presence of gonococci is either lacking or has not been sought. The discharge is most commonly whitish, mucous or muco-purulent, as a rule scanty and may yield yeasts or yeast-like organisms on culture. From dark-coloured discharge, a very rare condition, *Aspergillus*, *Penicillium* and other filamentous saprophytes have been isolated and they apparently impart their respective specific colours to the discharge.

Equally rare, is a reddish secretion from which Castellani has isolated, besides fungi, red pigment-producing cocci and bacilli.

The above-mentioned saprophytic species may be introduced during treatment, especially in the course of attempts at self-cure. In one such case *Fusarium* was found in the posterior urethra following an injection of cow's milk. The urethra may also be implicated by extension of thrush of the glans or it may be affected by any species thriving in the vagina.

CHAPTER VIII

EPIDERMOPHYTOSIS

General Survey

Under this comprehensive heading which combines both a clinical and an aetiological significance, various infections of an allegedly mycotic origin of the skin and its appendages will be discussed. Whether the organism incriminated in a given instance is the true primary cause or merely an invader of a host who has probably been previously prepared by sensitization or otherwise for its favourable reception by what is variously ascribed to allergy, gonadal activity or inactivity, vitamin deficiency, etc., is a debatable point. In the majority of cases the clinical picture differs in some details according to the fungus commonly isolated from the lesions, and the grouping of these into categories is either based on a similarity in their characteristics or on relationships that exist between their determining causes.

The following scheme of classification, although perforce artificial, is attempted in order to facilitate discussion of the different infections in a more or less organized continuity:

1. Lesions of the skin due mainly to members of the group *Trichophytoneae*, generally recognized as tinea or ringworm. They include the all important infections of the hairs and nails, in themselves appendages of the skin, and are inserted here for convenience.

2. Lesions in which pigmentation and depigmentation of the skin in patches constitute the main features.

3. Lesions in the skin and its appendages from which various organisms have been isolated, excluding the *Trichophytoneae*, and including members of the genus *Actinomyces*, yeasts, etc.

These infections are cosmopolitan but are generally more prevalent among communities in poor hygienic conditions and wherever there is close association with domestic animals, especially in rural districts.

1. *Lesions due mainly to members of the group Trichophytoneae*

Members of this group attack keratinized tissue, the horny layer of the epidermis, hairs and nails. Their predilection for keratin, a dead tissue to all intents and purposes, may be due just to that

peculiarity, and may also be because of an association with it of some chemical composition or change in the *p*H of the skin at the time of infection. The *p*H in hairy areas of the epidermis was found to vary from 6·2–6·5 before puberty to 4·5–5·6 soon after. Hormonal and probably other factors of an as yet inexplicable nature may also exert some influence, as may be seen in the advent of spontaneous cure, or at least the slower evolution, of some lesions in adults and of some ringworm of the scalp in children when they reach the age of puberty. The lesions produced fall into two categories:

A. Those confined to the epidermis.

B. Those occurring in hairs and nails, tissues allied to the epidermis proper, which usually escapes in their neighbourhood except for some scaling.

Lesions confined to the epidermis

These may be situated either in moist regions, inguino-crural, submammary and axillary folds, the vulva and the interdigital spaces, all belonging to the intertrigenous dysidroses, or on drier areas of the glabrous skin. The classical examples of mycosis of the natural skin folds is the eczema marginatum of Hebra, and the dysidrosiform affections of the interdigital spaces. On the drier parts of the glabrous skin, tinea circinata and herpes circinatus are the terms generally employed for the infections.

Pathological Properties of Genera of Trichophytoneae

Achorion Remak, 1845

Scutula or favic cup formation with little tendency to inflammation. Short lengths of mycelium arranged longitudinally mostly inside the hair. Kerion, sycosis and glabrous skin lesions.

Microsporum Gruby, 1843

Spores arranged in mosaic pattern mostly outside the hair and enclosing it as a sheath. Infected hairs left as short stumps. Hosts are domestic animals and man. Produces inflammatory lesions and folliculitis. Attacks glabrous skin, institutes kerion, sycosis and intertrigo.

Trichophyton Malmsten, 1848

Arthrospore formation in chains longitudinally disposed inside hair which eventually bursts at weakened spots and becomes vermiform and embedded in the scales either attached to, or

broken off flush with, the surface of the scalp. Glabrous skin lesions, sycosis.

Ectotrichophyton Castellani and Chalmers, 1919

Causes suppurative lesions of the horny epidermis and hair follicles. Surrounds invaded hairs with spores and mycelium. Sycosis, kerion.

Megatrichophyton Neveu-Lemaire, 1921

Produces dry sycosis with little tendency to inflammation.

Favotrichophyton Neveu-Lemaire, 1921

Produces animal pustular lesions, tinea tonsurans, herpes circinatus, onychomycosis, sycosis and kerion in man.

Endodermophyton Perry, 1907

Forms dry lesions of the glabrous skin without inflammation.

Epidermophyton Sabouraud, 1910

Attacks the horny layer of the epidermis only and not the hairs.

Eczema Marginatum of Hebra
" Dhobie Itch," " Tinea Cruris "

Definition. A moist epidermomycosis mainly of the inguinocrural region, and occasionally of the axillary or submammary folds, due to infection with members of the group *Trichophytoneae*, yeasts or yeast-like fungi.

Historical. In 1860 Hebra of Vienna described in detail the clinical picture of this infection in a manner which left no room for modification ever since. An original account including the fungous nature of the lesions was, however, first given in France by Devergie in 1857 and Hebra only improved upon it while adding fresh sites of possible infection, primary and secondary. In 1869 Pick repeated an earlier worker's experiments (Köbner, 1864) and confirmed the inoculability of the fungus, which was later (1871) further described and named by Harz. To Sabouraud goes the credit of cultivating it as early as 1895.

Aetiology. The following species have at various times been isolated from the lesions:

Epidermophyton floccosum (Harz, 1871) Langeron and Milochevitch, 1930 (=*E. inguinale* (Sabouraud, 1907) Sabouraud, 1910), (=*E. cruris* (Castellani, 1908) Castellani and Chalmers, 1910). This is the classical species.

E. rubrum Castellani, 1910; from Ceylon, proven experimentally.

E. perneti Castellani, 1910.

E. purpureum (Bang, 1910) Dodge, 1935.
E. rubidum (Priestley, 1917) Dodge, 1935.
E. salmoneum Froilano de Mello, 1921.
Endodermophyton concentricum (Blanchard, 1896) Castellani and Chalmers, 1910. Isolated in Egypt.
Microsporum ferrugineum Ota, 1921; from Japan.
Megatrichophyton nodoformans (Castellani, 1912) Neveu-Lemaire, 1921.
Syringospora cutanea Dodge, 1935, and other yeasts and yeast-like organisms.

FIG. 67. *Epidermophyton floccosum.* Colony on Sabouraud 2 per cent glucose-agar. (Original)

No age, sex or class is immune from infection, but, generally speaking, young adult males constitute the majority of sufferers. There is no reason to doubt that contagion plays a considerable part in the spread of the infection as cases sometimes reach epidemic proportions in families and larger institutions such as barracks, schools and universities. This is seemingly favoured by promiscuous use of towels, by means of underclothes washed *en masse* without proper boiling, hence the name "Dhobie" (Indian washerman) itch, and through contact with infected floors, seats and benches in swimming pools, gymnasiums, shower-bath cubicles, etc., while sexual contagion is also of common occurrence. Predisposing causes have been sought for, and it would seem that excessive

perspiration, a sodden state of the part concerned, together with skin of a higher degree of acidity than normal are essential conditions for the fungus to take root. Post-pubertal hormonal and chemical changes are probably part of the determining causes which may explain the rarity of infection before puberty. The liability of soiling with urine and semen of the usual site of election may be put forth as providing rich ingredients for the fungus to thrive in.

Symptoms. The site of election is usually the ano-inguino-crural area, but other situations, the submammary folds, especially in obese subjects, and the axilla may be involved in primary lesions or secondarily. The left side on the inner side of the thigh where it is in contact with the scrotum is more commonly affected especially among wearers of trousers, probably because of the prolonged apposition of the parts mentioned. This is in contrast with what happens among natives who wear gowns, in whom both sides are equally susceptible to attack. It may begin like an intertrigo or, more commonly, the infection is first heralded by intense pruritis and the formation of a small, round and elevated reddish area. This soon pales in its centre, which later becomes hyperpigmented, while the circumference, in which the activity of the fungus is most pronounced, grows larger and becomes more irregular in outline. Distinguishing features about the border of the patch are that it is usually red, slightly elevated, sharply defined and festooned. The next stage in the evolution of the lesion takes place along the edges, where an eruption of small vesicles is seen. After a short time they burst open and their serous contents dry up as surface crusts. Scratching continues and denudes the lower layers of the epidermis in parts, and a picture is formed of punctiform and larger raw areas, together with scattered brown crusts of mixed blood, serum and dead

FIG. 68. *Eczema marginatum* of Hebra. "Dhobie itch." *Tinea cruris.* (Original)

epidermal cells. If untreated, the lesions will spread by auto-inoculation of fresh areas in the vicinity where they go through the same cycle and eventually merge into one another. Contact with the opposite thigh leads in time to the formation there of an area more or less symmetrical in outline with the original. Extension may implicate lower regions of the thigh, the gluteal and anal folds, and rarely the scrotum and penis, shaft and glans, or labia majora, while spread in an upward direction may reach the pubis and even higher on the hypograstrium as far as the umbilicus. The submammary and axillary folds may occasionally show coincidental lesions presumably the result of auto-inoculation. Generalization over the body through scratching is possible, the nails becoming infected in the process. With treatment, healing begins in the centre where the skin regains its healthy appearance except for some brown discoloration which gradually disappears in its turn. Secondary infection from scratching may lead to a moist eczematoid condition which seems to help in hastening the progress of healing under treatment.

Uncommon forms of eczema marginatum are occasionally met with. An appearance suggestive of pityriasis rosea, but more inflammatory, may be seen, in which the contrasting red edges are not present and the whole lesion is uniformly angry-looking and covered with fine powdery scales, while in another a still more inflammatory reaction is produced in patches which are distinctly elevated above the surrounding normal skin and covered with crops of vesicles and pustules. A similar form is reported by Castellani as having thick elevated margins with deep-seated nodules along them resembling blind boils. In this type, the hair follicles are also attacked. Yet another atypical lesion is known which can only be differentiated from erythrasma after cultivation of the organism responsible.

Diagnosis. The festooned, sharply-defined, red, slightly elevated borders of the lesion are characteristic, especially when taken in conjunction with the site involved. Intertrigo is a likely source of error, but it lacks the above-mentioned characters and presents a raw surface laid bare by absence of the upper layers of the epidermis, and exudes a whitish turbid fluid. In eczema the secretions are yellow serum or sero-pus which do not dry into crusts when the lesions are intertrigenous. Erythrasma patches possess margins of a darker hue than those of eczema marginatum and the desquamation of the lesion is furfuraceous.

Microscopic examination of the scales from the advancing borders

will clear any doubt as to the nature of the infection, although only a few scattered spores, if any, are discovered when a chronic, secondarily infected case is in question.

In culture, colonies of *Epidermophyton floccosum* are greenish-yellow, small, elevated at centre, dry, velvety, powdery, with radial furrows increasing in number with age. Pleomorphism sets in in 3–4 weeks but can be avoided by using Sabouraud's conservation medium, on which the colony is citron yellow, powdery, broadly umbilicate at centre, and with irregularly elevated margins. Mycelium septate, ramified, 3–6μ in diameter, tips swelling into closterospores singly or in groups up to seven, closterospores 20–35 $\times$ 6–8μ, averaging 4–5 cells, with thin walls, sessile, or the basal cell elongates like a pedicel.

Treatment. Unless energetically treated, the infection will run a chronic course, and apparent healing is often belied by recurrence, especially with the advent of the warmer weather and increased perspiration. In early mild cases, uncomplicated by eczema, the mere application of weak tincture of iodine diluted five times in 70 per cent alcohol effects a cure in a short time. Swabbing with a 2 per cent aqueous solution of mercurochrome 220 once and subsequently twice *per diem* is also effective. No bandaging is necessary. Zinc oxide ointment may be smeared over the area after the application of iodine to prevent contact and rubbing of diseased surfaces of the skin. Calamine or lead subacetate lotions may be necessary to allay itching every now and again. In more advanced cases, 2 per cent salicylic acid in 75 per cent alcohol should be applied twice daily to the lesions, and a benzoic-salicylic ointment rubbed in nightly. A resorcin-salicylic ointment is also recommended. Refractive and severe infections yield to chrysarobin (1 per cent in zinc oxide ointment). The toxic effect of this drug must, however, be borne in mind. Its contra-indications will be discussed later under the heading of fungicides. If the lesions are eczematized, attention is at first directed at combatting the eczema. In its vesicular or weeping stage, lead subacetate lotion or glycerine of borax may be employed, but the dressing should be kept constantly moist. In its second phase Lassar's paste is used. If the salicylic acid proves too

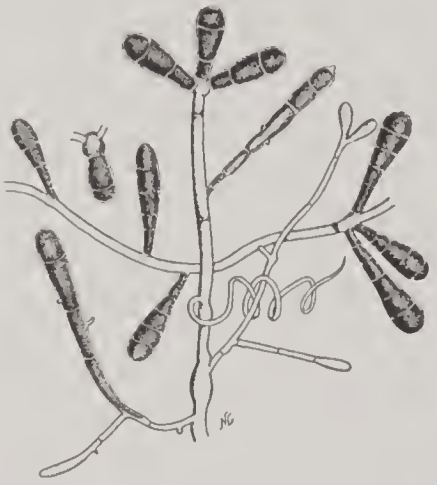

FIG. 69. *E. floccosum*. Cultural morphology. Terminal and lateral closterospores and spirals. (Original)

irritating, it may be withdrawn and a little lanolin added. In chronic cases 2–5 per cent of ammoniated mercury may be incorporated in Lassar's paste.

For prophylaxis, the clothing in institutes or where mass washing is done should be thoroughly boiled and the promiscuous use of towels discouraged. The patient's washing and personal towels must be done separately to avoid contagion. Recurrences are frequent and necessitate a close watch for any suspicious signs which are an indication for the resumption of treatment which, in any case, should be continued for some time after apparent cure.

Erythrasma

This following condition is mentioned here because of its similarity to *eczema marginatum* in site, although its aetiology should bar it from this section.

Definition and aetiology. Erythrasma is a widespread but mainly tropical mild chronic type of dry epidermomycosis of the genito-crural regions due to infection with *Actinomyces minutissimus* (Burchardt and Baerensprung, 1859) Brumpt, 1927. *Actinomyces pinoyi* (Froilano de Mello and St. Antonio Fernandes, 1919) Dodge, 1935, has also been isolated from a case diagnosed clinically as erythrasma. De Michele, Ducrey and Reale obtained a culture which reproduced the clinical picture when inoculated into healthy human skin.

Symptoms. The affection manifests itself in the form of circumcribed areas, more or less rounded with scalloped borders, dull red or brownish in colour, slightly elevated above the level of the surrounding skin and often checkered with minute folds. The surface of the lesions is covered with fine, powdery scales, usually dry, but sometimes moistened with perspiration. Although the site of election is one or both of the genito-crural folds or the internal aspects of the thighs, the infection may spread to the pubic region or down to the anterior aspects of the thighs, or it may occur primarily but less commonly so in the axillary, submammary, popliteal, cubital or abdominal folds, especially in obese subjects.

The main complaint is a moderate amount of pruritis, periodically aggravated by perspiration and heat. More adult males than females are affected with erythrasma, and no cases have so far been reported from children.

Diagnosis. Clinically, the infection is likely to be mistaken for intertrigo, trichophytosis, tinea cruris or pityriasis versicolor. Under the microscope the scraped scales will be found to contain the parasite as fine mycelial filaments, under or hardly exceeding 1μ in diameter, usually unbranched, straight or curved and easily fragmenting into short bacillary lengths of about 10μ each. The hyphae may sometimes take the form of very short segments or even of coccus-like fragments. Attempts to grow the fungus from scales is, more often than not, attended with failure.

Actinomyces minutissimus is an aero-anaerobe giving when culture is successful a brown growth on gelatin, wine red on potato and brownish-red on agar. Culture is unknown on liquid media.

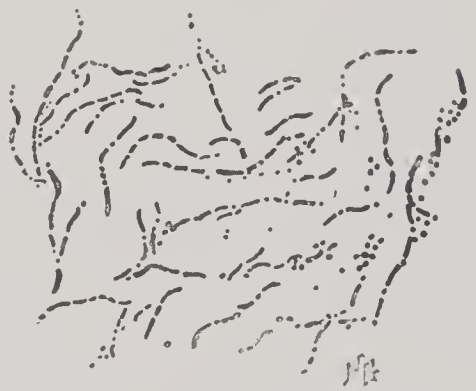

FIG. 70. *Actinomyces minutissimus*. Appearance in the scales in erythrasma. (Original)

Treatment. Light and loose cotton underclothing and frequent baths with non-irritating soap are recommended. Painting the affected areas with 1 in 10 tinctura iodi mitis or with a 1 in 1,000 solution of potassium permanganate several times daily often brings about a cure. Sulphur, chrysarobin or resorcin ointments are equally as effective, but the treatment must be persevered with for some weeks even after apparent cure.

Interdigital Mycosis

Definition. Interdigital dysidrosiform erosions often spreading to the soles or palms brought about as in "Dhobie itch" by members of the group *Trichophytoneae*, mainly species of *Epidermophyton*, or by yeasts and yeast-like fungi.

Aetiology. The following species have been isolated from primary interdigital lesions or from their secondary extensions in neighbouring or remoter parts.

Epidermophyton interdigitale (Priestley, 1917) MacCarthy, 1925. The more commonly isolated species.
E. floccosum (Harz, 1871) Langeron and Milochevitch, 1930 (= *E. inguinale* (Sabouraud, 1907) Sabouraud, 1910).
E. pedis (Ota, 1922) Dodge, 1935.
E. niveum MacCarthy, 1925.
E. gypseum MacCarthy, 1925.
Trichophyton chosenicum Takahashi, 1925.
Corethropsis hominis Vuillemin, 1913.

Saccharomyces intertriginis Touraine and Devaux, 1923.
S. sternoni Sartory *et al.*, 1932.
Cryptococcus jeanselmei Burnier and Langeron, 1922.
Debaryomyces fabrii Ota, 1924.
Blastodendrion gifuense (Taniguchi, 1926) Dodge, 1935.
Syringospora cutanea Dodge, 1935.
S. negroni Dodge, 1935.
Actinomyces keratolyticus Acton and McGuire, 1931.

Non-mycotic lesions seem to occur very frequently, cases in which no mycotic elements could be demonstrated. In these instances bacterial infection, mainly staphylococcal, often accounts for the intertrigo of the toes.

Infection is more commonly met with between the toes and generally prevails among the same subjects and under the same conditions as in eczema marginatum. Constant immersion of the hands in water and subsequent mycosis between the fingers have led to the creation of the term "Jewish washerwomen's disease," which is probably brought about by the women refraining from the use of soap with its fungistatic alkalinity, because of religious prejudice in fear that the fat employed in its manufacture may have originated from non-kosher animals. A similar mycosis is reported by Taniguchi (1926) among paper workers whose hands are nearly constantly wet, and *Blastodendrion gifuense* was isolated from the particular preparation used in paper making and from the lesions on the workers themselves. "Surfer's foot" is also a recognized clinical condition in Australia where surf-riding is commonly practised. "Athlete's foot," another term for the lesions, denotes the predominance of the infection among young athletic males. Swimming pools seem to provide constant reservoirs of infection, and unsanitary habits, improper hygiene and infrequent change of socks and the persistence of the fungi in the shoes are among the more important causes. Whether rightly or wrongly, the infection is ascribed to these various predisposing causes, and they at least possess one feature in common, namely, moisture of the epidermis to the point of maceration which favours the growth of the parasite. Further sources of infection, probably of an accidental and infrequent nature, may exist and operate in everyday life. As an illustration, Trichophytons have been isolated from the handles of golf clubs in a miniature golf course On the other hand, the organisms have been grown from the skin of apparently normal feet.

Symptoms. Asymptomatic lesions occur, of which the patient remains in ignorance and only discovers by accident, or when they

become chronic or spread to the dorsum or sole of the foot and are secondarily infected. In this type, in contrast with the symptomatic lesions, pruritis, the main subjective sign, is absent. When it does occur it soon attracts attention by its periodically persistent character. At this stage the horny layer of the epidermis, usually in the folds between the toes, appears thin, shiny, and of a reddish-brown colour, or else greyish-white, moist, and slightly thickened. Later it becomes macerated, eroded, and capable of being easily peeled off together with the underlying layers of the epidermis as thick sodden sheets, leaving a raw, sore surface underneath. Often a brick-red pruritic line may exist along the outer margins of the lesions on two adjacent toes between their normal dorsal surfaces and the whitish epidermis of their opposed sides. The lesion seldom encroaches on the dorsal aspect of a toe or over the sole, but occasionally there may be an extension of the damage amounting to a cleft in the web between the affected toes or in their plantar folds. The pruritis is usually more marked on the edges of the lesion rather than in the folds where only soreness is felt. A marginal vesicular eruption is in some cases an associated feature. The toes are more commonly affected than the fingers except when the person's occupation entails prolonged immersion of the hands or feet in a liquid medium. The species isolated from between the fingers are usually of the group *Monilia*, and cause the common "erosio interdigitale" of the webs of the fingers, while members of the *Trichophytoneae* restrict themselves more or less to the toes. Secondary infection complicates a fair number of cases, especailly where the toes are involved, and may even lead to lymphangitis spreading up the leg with inguinal lymphadenitis, sometimes before secondary infection complicates the case. Recurrence

FIG. 71. Interdigital mycosis, advanced case with pronounced erosion. (By courtesy of N. F. Conant)

after apparent healing of the lesions is to be borne in mind as a common occurrence when the warmer weather sets in.

Diagnosis. Itching between the toes with hyperiderosis and maceration of the epidermis, especially in young, active and athletic subjects probably living in an institute or bathing frequently in public baths, should always raise a suspicion of fungus infection. This may be confirmed by demonstrating the parasite in scrapings from the lesion as mycelial filaments.

FIG. 72. *Epidermophyton interdigitale*. From foot. Colony on Sabouraud glucose-agar. (By courtesy of N. F. Conant)

On glucose-agar, a colony of *E. interdigitale* suggests a piece of blotting paper with a central velvety boss surrounded by a buff area and a white periphery; the reverse is chestnut-brown with a yellowish periphery. Several variants of the species are reported. Multiseptate closterospores, compound thyrses of aleurospores and spiral hyphae are present and chlamydospores are found in old cultures.

Colonies of *E. pedis* are small, elevated in the centre, yellowish-cream in colour, and the reverse is violaceous or brownish. Pyriform aleurospores on simple hyphae or on compound thyrses and chlamydospores in older cultures are seen.

Treatment. Prophylactic treatment is very important in epidermophytosis of the toes, which often proves very persistent. Eradicating the parasite locally should if possible be supplemented by tracing and dealing with the source of infection. In some public baths, troughs, depressions or canals are provided containing solutions of 10–15 per cent sodium thiosulphate or 1 per cent sodium

hypochlorite through which bathers have to wade to get to the pool. This attempt at eliminating fungus infection through contagion in the public water, or at least at decreasing its incidence, has been attended with encouraging results. Foot hygiene in the way of frequent change of socks and daily washing and thorough drying of the feet and interdigital spaces, especially in hot weather, is an

FIG. 73. *Epidermophyton gypseum.* From foot. Colony on Sabouraud glucose-agar. (After N. F. Conant *et al.*)

effective measure in the case of persons predisposed to infection because of hyperiderosis. The interdigital spaces and the toes should afterwards be lightly painted with weak tincture of iodine or dusted with talc and boric acid powder. The likelihood of shoes acting as a reservoir of infection may be counteracted by fumigating them with vapour of formaldehyde. Ventilation of the feet through the use of cotton socks and avoidance of rubber shoes, preference for sandals or shoes with open uppers are necessary for freely perspiring feet. Paper slippers to prevent contact with possibly infected bath floors, easily cleaned rubber floor mats, the abolition of stools and benches during drying and the use of personal towels are effective prophylactic measures.

In the earlier stages of infection dilute tincture of iodine may be

employed followed by the application of zinc oxide ointment. Potassium permanganate baths (1 in 1,000) or a 2 per cent alcoholic solution of salicylic acid may be tried. Painting with stronger solutions of permanganate of potash (1 or more per cent) or with 2 per cent silver nitrate are sometimes effective, although the latter is painful for a short time after its application. Such strong measures however, should always be practised with care. The application at bed-time of ichthyol ointment (20 per cent) is soothing and ensures continuous fungicidal action during the night. In cases with no eczematous complications, Taylor (1930) found out that intense cold from vaporization of ethyl chloride could bring about a cure. Every other day the ethyl chloride jet is directed at the infected area and for about half a centimeter beyond it for a period of half to one minute until the skin goes dead white. Six such sittings are usually curative. Following the first application the pruritis is greatly alleviated and intense desquamation ensues.

Eczematoid complications are dealt with as described in the treatment of tinea cruris.

Epidermophytosis of Hands and Feet
Dysidrosis

The thick epidermis of the soles more commonly, and of the palms less often, may be attacked by extension from phytosis of the digits, or it may be the site of primary infection. Another type of lesion is sometimes seen in the form of epidermophytids, probably an allergic manifestation following upon infections in other parts of the body.

On the hands, the lesions, occurring mostly in young and middle-aged persons of both sexes, are usually unilateral and are heralded by local pruritis, tingling and burning sensations before they appear as pin-head or lentil-sized vesicles deep under the epidermis. They are situated as a general rule on the lateral aspects of the middle and distal phalanges which seem to be the site of election in early infections, but may also form in the interdigital spaces, at the bases of the fingers, on their dorsal and palmar surfaces, especially in recurring or chronic cases, or elsewhere on the palm. These vesicles, which are produced through the epidermis being raised and separated by the underlying fluid contents, are at first discrete and variable in number and can just be felt above the surrounding skin. In appearance they are suggestive, at the beginning, of boiled sago grains because of their translucent contents which, however, turn to grey, steel-blue,

yellow, or to a reddish or a pale brown colour. In some cases, even while the vesicles are forming and before pyogenic infection takes place, the patient may complain of pain along the lymphatics of the arm draining the part affected, and there may actually be some enlargement of the axillary glands. Confluence of neighbouring vesicles into fairly large bullae is occasionally seen, but the general

FIG. 74. Epidermophytosis of the palmar aspect of the hand. *Dysidrosis lamellosa sicca.* (Original)

FIG. 75. Epidermophytosis of the dorsum of the hand. (Original)

rule is for the small isolated ones to dry up in a day or two and for their tops to peel off exposing pink, raw surfaces. Surrounding the vesicles throughout their evolution there is very slight or no erythema. Crops recur irregularly in this fashion over very long periods, sometimes every few days, and as they dry up and heal spontaneously they become covered with delicate pink fresh epidermis which changes into slightly pigmented maculae. Instead of drying up, the vesicles, discrete or confluent, may burst automatically or through scratching

and discharge their fluid contents, and there forms a more or less extensive area or areas with irregular borders of overhanging fringes of epidermis, a condition bearing the label of *dysidrosis lamellosa sicca*. Underneath these peripheral tags of epidermis, fresh vesicles may sometimes form and lead in time to further enlargement of the exposed surface of the lesion. The fluid collecting in the vesicles may be serous, albuminous, acid or alkaline, and is of a sticky consistency in which fungus elements cannot be easily, in fact very seldom, demonstrated. Instead of vesicles, painful pustules surrounded by inflamed zones may be formed, or there may be a combination of both vesicular and pustular lesions.

On the soles, the vesicles form under a depressed epidermis, contrary to what occurs on the palms, and the lesions follow the same course already described except for a greater tendency to extension and secondary infection.

Lesions without the initial vesicle formation are also met with on the palms and soles and institute a picture of hyperkeratosis, desquamation, cracking in the natural folds of the skin which peels off in thick flakes and, in a few instances, subsequent secondary infection. The general course, however, in such cases is for the lesions to remain perfectly dry and uncomplicated. The condition recognized under the term "cracked heel" is an example of this type of infection, but is due to an actinomycotic aetiology and will be dealt with separately. Occupation has in some cases a bearing on liability to infection favoured by chronic irritation and prolonged immersion in water, etc. Patients often include washerwomen, bakers, masons and printers.

Species of the group *Trichophytoneae* isolated from the above-mentioned dysidrotic or pseudodysidrotic lesions include the following:

Trichophyton tonsurans Malmsten, 1845 (= *Tr. crateriforme*, Sabouraud, 1902).
Tr. sabouraudi Blanchard, 1896 (= *Tr. acuminatum* Bodin, 1902).
Epidermophyton interdigitale (Priestley, 1917) MacCarthy, 1925.
E. niveum MacCarthy, 1925.
E. gypseum MacCarthy, 1925.
E. plurizoniforme MacCarthy, 1925.
E. persicolor (Sabouraud, 1910) Dodge, 1935.
E. cerebriforme Dodge, 1935.
Favotrichophyton violaceum (Sabouraud, 1902) Dodge, 1935.
F. ochraceum (Sabouraud, 1908) Neveu-Lemaire, 1921.
Ectotrichophyton mentagrophytes (Robin, 1853) Castellani and Chalmers, 1919.
Microsporum audouini Gruby, 1843.

Diagnosis. This is best accomplished on microscopical examination in spite of the rarity of positive findings. The portion of epidermis covering an unburst vesicle is snipped off and examined in a clearing agent, keeping the palmar surface downwards on the slide. Cheiropompholix of Hutchinson, a non-inflammatory condition bearing a strong resemblance clinically to epidermophytosis of the hands, is to be excluded in differential diagnosis. It is spontaneous, of sudden onset, and presents a bilaterally symmetrical vesicular or bullous picture, occurring mainly on the palms, but the soles and digits may also be affected. Erythemato-squamous eczema and psoriasis palmaris may also be confounded with mycotic infection. The psoriasiform eruptions occur during the intermediate stage between secondary and tertiary syphilis and can be diagnosed on other conclusive evidence.

Treatment. Non-irritating lotions and fungicidal ointments are employed, varying the course to suit the severity of the lesions and the presence or absence of eczematous changes and secondary pyogenic infection.

Infections of the fingers and palms often respond to autogenous vaccines from the organisms of infected vesicles which are opened aseptically. Staphylococci and streptococci are usually found. Two prolonged courses of injections within six months with an interval of two months is advocated.

Atebrin $1\frac{1}{2}$ gr. t.d.s. for five days, a similar period of rest, followed by a repetition of the atebrin course has met with remarkable success.

The following two types of infection, although caused by Actinomyces, are included here on anatomical grounds.

Keratodermia Plantare Sulcatum
" Cracked Heel "

Definition. An actinomycotic infection of the plantar surface of the foot, rarely occurring on the palm, producing marked lysis of the skin and leading to the formation of cracks and pits, often extending to the toes and sometimes causing paronychia and onychomycosis.

History, aetiology and geographical distribution. The disease was originally described by Castellani in Ceylon, but it is also present in India, Central Africa and Egypt. *Actinomyces keratolyticus* Acton and McGuire, 1931, is the causative organism, confirmed as such by voluntary human inoculation and by its subsequent recovery

from the experimentally infected tissues. It has also been isolated as a saprophyte in nature from horse and cattle dung.

Symptoms. The thickened skin of the sole presents fairly deep fissures and holes produced by the keratolytic action of the organism, usually beginning at the heel and spreading forwards to the ball of the foot at the base of the big and first toes and thence to the interdigital spaces; or the infection may on the other hand start at the toes and travel in the opposite direction. The primary lesion is generally in the form of a pit or crack which develops into an ulcer on the heel, at the base of the big toe or in the first interdigital space. In these two latter situations an initial pruritis is followed by the appearance of a deep fissure which changes into an extensive and extremely sensitive ulcer with a well-raised margin and a dull red floor, the condition described by Castellani from Ceylon as "ulcus interdigitale." There is no surrounding inflammation and the discharge, if present, is scanty, but a sodden state of the folds of the skin all round the lesion is often noticed. Extension may lead to paronychia and onchyomycosis with cracking, brittleness and pitting of the nail.

Bare-footed natives and gardeners treading in manure are most prone to the infection which is favoured by the dampness of the soil during the wet season when the condition gets worse after amelioration in the drier months of the year. The disease runs a chronic course and persists several months with probable aggravation of the lesions, necessitating in some cases actual amputation of seriously involved toes.

Diagnosis. The deep sulci and the pitted, sieve-like appearance of the thickened epidermis are pathognomonic and distinctly different from the changes seen in syphilitic or framboesial affections of the sole. In the tissues, the mycelium is found in the shape of fine non-septate filaments, about $0{\cdot}8\mu$ in diameter, or so closely septate as to look like chains of cocci. Cultures on Norris' agar are easily obtained from the lesions.

Treatment. This is instituted with a preliminary thorough cleansing with soap and warm 1 per cent solution of carbolic acid. Frequent washing with the same or a similar weak antiseptic lotion and the application of ointments of salicylic or boric acid produce good results. A certain amount of rest should also be recommended.

Erysipeloid Dermatitis

Definition. A contagious form of actinomycotic dermatitis mainly of pigs and cattle but sometimes affecting man by transmission from animals. On rare occasions, the ingestion of infected and insufficiently cooked meat, some fishes or edible crustaceans may also lead to an intestinal type of the disease.

Aetiology and history. The parasite, *Actinomyces erysipeloides* (Neumann and Lehmann, 1896) Lachner-Sandoval, 1898 (synonyms: *Oospora erysipeloides* Neumann and Lehmann, 1896; *Streptothrix rosenbachii* Kruse, 1896; *Pasturella thuillieri* de Toni and Trevisan, 1889, etc.), was first discovered in pigs by Pasteur and Thuillier in 1883 and by Rosenbach in man in 1884. It exists in nature as a saprophyte on a variety of fishes and crustaceans sold for human consumption, on animal bones used for industrial purposes and, according to Klander (1932), generally on a number of animals and vegetables, either when they are alive or when in a state of decomposition. Bacillus rhusiopathiae is the bacteriological name for the organism.

Symptoms. The infection is contracted while attending diseased animals or handling their carcases or, as has occurred to some workmen in the United States, in manufacturing buttons from infected bones.

After a very short incubation period of one or two days following upon the introduction of the fungus, as a rule through a cut or an abrasion of the skin, the infection manifests itself as a mild dermatitis of an erysipeloid nature which may cause constitutional disturbances with fever, sometimes accompanied by rigor and pains in the joints, rarely developing into arthritis and synovitis as late complications. Normally, if it does not become generalized, the course ends in spontaneous recovery in two or three weeks' time. One attack often confers a lasting immunity.

Diagnosis. Clinically, the diagnosis may be guessed at from a consideration of the patient's occupation or from a history of exposure to infection. A skin reaction test by intradermic injection of dried cultures of the fungus has given positive results in one case reported by Lemierre in 1933. The parasite as described by Rosenbach occurs in the lesions as sparsely ramified slender entangled hyphae in bacilliform lengths, straight, wavy or spiral, with an occasional terminal swelling. Cultures are easily obtainable.

Treatment. This is conducted on symptomatic lines, and local measures with iodine preparations, ichthyol ointment, etc., can be prescribed. The infection may respond promptly to a few hundred thousand units of penicillin within two or three days.

Lesions on the Drier Areas of the Epidermis
Tinea Circinata

The exposed parts of the body are usually, but not invariably, the sites of infection with the circinate lesions of dermophytes. The neck, upper arm, wrists, shoulders and legs are favourites.

FIG. 76. *Tinea circinata* patches on the back of the neck. *Epidermophyton persicolor* infection. (Original)

The fungus is mostly derived from, and in the course of association with, domestic animals on farms, in the country, and in the homes in cities where pets are kept. Secondary patches from remote or neighbouring lesions on the scalp or elsewhere may also occur, the offending organism being, as a rule, a member of the group *Trichophytoneae*, including *Achorion schoenleini* of favus, as well as the species of the genera *Epidermophyton* and *Trichophyton* and their allies, and of *Microsporum*.

FIG. 77. *Tinea circinata* of the neck. *Epidermophyton floccosum* infection. (Original)

FIG. 78. Eczematized *tinea circinata* of the hand. (Original)

The patches of tinea circinata follow common lines of development, spreading in a widening circle and tending to heal spontaneously through the death of the fungus in the centre which later becomes hyperpigmented. The border, on the other hand, where the organism is most active, is of a red colour of varying intensity, while dry scales, small or large, cover the patch, especially on its older portions where they are more easily scraped or naturally fall off.

Herpes Circinatus

This is a modification of the above-mentioned type of lesion in which vesicles are formed haphazard on the patch, or just inside the

FIG. 79. Trichophytosis of the glabrous skin due to infection with *Favotrichophyton discoides*. Lesions of a characteristic pattern suggestive of *pityriasis rosea* and with slight inflammatory reaction. (Original)

advancing ring which consequently appears hyperaemic and oedematous. The vesicles may change into pustules and the hair follicles may become infected, in which case their walls are thickened and they may contain spores. The vesicles or pustules eventually burst open, are replaced by scabs, and healing accompanied by pigmentation finally takes place from the centre of the patch outwards.

FIG. 80. Trichophytosis of the glabrous skin due to infection with *Favotrichophyton album*. Lesions of a pattern suggesting *pityriasis rosea* with inflammatory and pustular reaction. (Original)

FIG. 81. *Herpes circinatus*. (Original)

FIG. 82. Eczematized *herpes circinatus*. (Original)

Pruritis, a common feature, leads to local secondary infection, lichenification of the patch and conveyance of fungus elements to neighbouring or remoter areas of the skin by means of the nails which in their turn may become involved during the transfer. Allergy also plays an occasional part in the development of secondary patches as phytids which will contain no evidence of mycelium or spores.

In the original lesions of tinea, the fungus elements are frequently seen in the scales, especially nearer the borders of the patch and in

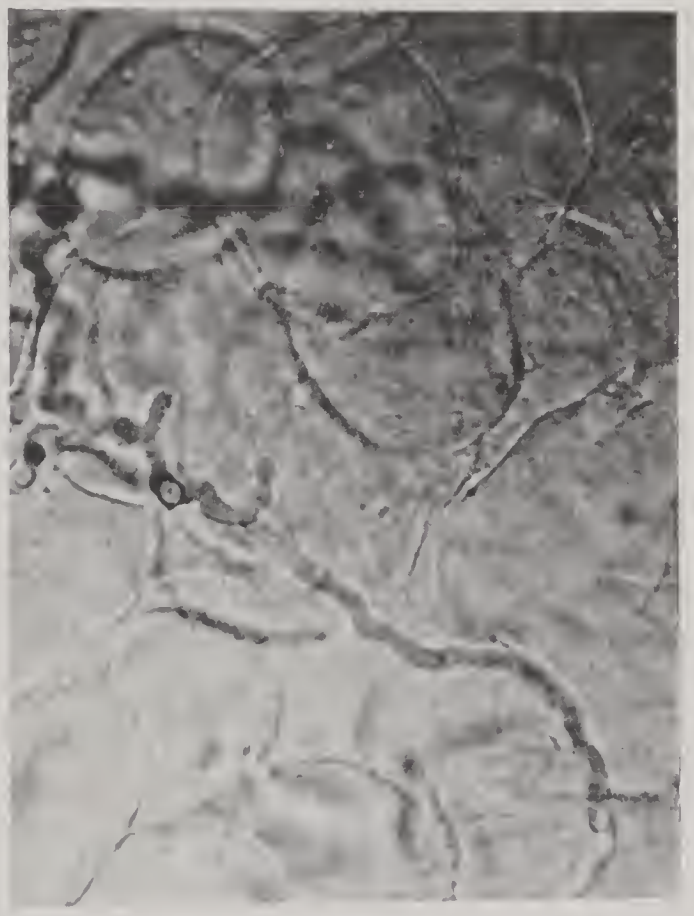

FIG. 83. Fungus elements : spores and mycelium in epidermal scrapings. (Original)

comparatively early infections. They soon cease to be easily demonstrable with chronicity and the changes it entails.

Favus of the Glabrous Skin

Involvement of the skin with favus may be primary or secondary by extension from the scalp. The lesions, termed *favus herpeticus*, resemble tinea circinata patches of trichophytic or other aetiology, but are more regularly rounded. They are apt to occur on any part of the glabrous skin, but the scrotum seems to be a fairly common

site. Typical favic cups are occasionally seen and lesions are apt to become confluent in neglected cases and may cover quite extensive areas. Generalization of the infection is known to have implicated mucous surfaces and lymphatic glands. *Achorion schoenleini* has been isolated from the blood of such cases.

Diagnosis is arrived at by finding mycelium and spores in epidermal scrapings followed by their culture.

FIG. 84. Favus of the glabrous skin. Arm infection. Note scutula. (Original)

FIG. 85. Favus of the body. Multiple godets (sulphur cups) on the back. (Original)

Treatment. Body favus is easier to treat than hair favus. Godets may be softened with moist antiseptic dressings, the lesions are scraped off with a spoon and tinctura iod. mit. is applied at two-day intervals. Watch should be kept out for recurrences.

Diagnosis of Tinea Circinata

Careful examination of the rest of the body for evidence of primary foci of infection, especially on the scalp, should not be neglected. The likelihood of an animal source of infection either in the home or in connection with the patient's occupation should also

be borne in mind. The circinate lesions, progressing peripherally, their desquamating character, the slightly erythematous margins, and in more advanced cases the central healing and light hyperpigmentation are important features. Obviously, mycelial elements when discovered microscopically in the scales from the borders of the lesion where the parasite is most active, would clinch the diagnosis.

Conditions to be taken into account in differential diagnosis include pityriasis rosea of Gibert, psoriasis, circinate syphilides, etc. Pityriasis rosea begins with a large "herald patch" or *plaque primitive* which is larger than any subsequent lesion and appears on the thorax, upper part of the lateral aspects of the neck or high up on the limbs. The patches are more or less circular and scaly with sharply-defined borders. The history reveals the sudden spread of the eruption symmetrically downwards over the extremities and trunk, stopping, however, short of the wrists and ankles. The patches are larger in number when the affection is fully developed, and each possesses an external pink margin, slightly elevated, and a fawn-coloured centre which shows typical fine wrinkling. Some constitutional disturbances, mild pyrexia and sore throat might accompany the onset of the eruptions. In psoriasis the scales are large, fairly thick, silvery-white and relatively adherent, overlying red, easily bleeding surfaces. Their distribution is commonly on the extensors of the limbs at the elbows and knees. Circinate and scaly syphilides are recognized by their brown colour, small size and slight scaliness as well as by concomitant specific evidence.

Treatment of Tinea Circinata

The lesions of tinea circinata, including favus of the glabrous skin, are comparatively amenable to effective treatment. A few applications on the patches of dilute tinctura iodi mitis (1 in 5) are generally successful. This, however, is not without its exceptions, and several trials may have to be made with fungicidal ointments (Whitfield's for preference) and lotions before cure is accomplished. In cases complicated by secondary infection and eczematoid changes, the appropriate measures enumerated under eczema marginatum are recommended.

Mycological Diagnosis of Dry Skin Lesions

As the dry skin, whether normal or the site of a lesion, is hardly free from deposits of aerial spores and bacteria, it is as well to exclude these elements from the pathological material under examination,

particularly the bacteria which often overgrow, or inhibit the growth of fungus colonies on culture. The first procedure to that end is to clean the lesion and its surroundings with 96 per cent alcohol. The skin lesion is then scraped with shaving movements by means of the knife shown in Fig. 86 or by a sharp-edged scalpel or safety razor blade until serum begins to ooze out. It is to be borne in mind that in epidermophytosis the fungus elements exist in the superficial horny layers of the epidermis and, more important still, that they are more active and more easily demonstrable at the periphery of the lesion. The scales are caught on a flamed slide or a convenient sterile receptacle like a Petri dish. They may either be left to dry for a week between flamed slides before culture to minimize the risk of contamination, or this may be done more quickly by washing them in absolute alcohol which is allowed to dry with them in a few minutes. Some of the scales collected are examined forthwith under a cover-slip in chloral lactophenol, plain water or 30 per cent KOH for evidence of spores or mycelium. The rest are then inoculated on Sabouraud's 4 per cent agar slopes or, if in a Petri dish, some of this medium, liquefied in a water-bath for the occasion is poured in a thin film over them. When the colonies begin to appear, and before they grow big enough to overlap one another, suspicious ones are transferred on to Sabouraud slopes. These methods are applicable with few, if any, modifications in practically all superficial lesions of the skin and its appendages. Incubation in these cases is usually at 25° C. or at room temperature in the summer.

FIG. 86. Instruments for the collection of hairs and epidermal scales for examination and culture. From left to right: Inoculation nickel-chrome wire (note angle and tip hammered flat), epilation forceps, dissecting, teasing and scraping knife and for picking embedded hairs. (Original)

Tinea Imbricata
"Tokelau" (Samoa)

Definition. A chronic, contagious, pruriginous dermatomycosis characterized by the production of overlapping, more or less

triangular scales over lesions that trace in typical cases concentric intricate designs.

History. Manson, who introduced the term "tinea imbricata" after describing the causative fungus in the desquamations in 1872, gave the first clear account of the infection and the mechanism of its evolution, and succeeded in reproducing the lesions experimentally in man. Since then, further studies by various workers—Nieuwenhuis (1898), Castellani (1910), Hanawa and Nagai (1917), Dubreuil (1919), and others—confirmed and enlarged upon Manson's findings and introduced more species as aetiological agents.

Geographical distribution. This is roughly restricted by latitudes 25° N. and 30° S. It exists in India, Ceylon and the Malay Peninsula as a western limit, in southern China and Formosa to the north, the Philippines to the east, and in New Guinea, Borneo and Java to the south, including the rest of the East Indian Archipelago. Farther east, more endemic centres are present in the islands of the South Pacific, especially the Gilbert, New Hebrides and Fiji Islands, and to a lesser degree in Brazil and other parts of tropical America. Cases have also been recorded from Egypt and South Africa.

Aetiology. Three species of the genus *Endodermophyton* are so far known to be responsible for the disease:

Endodermophyton concentricum (Blanchard, 1896) Castellani and Chalmers, 1910.
E. indicum Castellani, 1911.
E. tropicale Castellani and Chalmers, 1919.

Endodermophyton concentricum, Manson's species, discovered by him and named by Blanchard in 1896, is the classical aetiological agent. *E. indicum*, of common occurrence in Malaysia, was isolated by Castellani from a few cases of tokelau in Ceylon, but is considered like *E. mansoni* which was also isolated by Castellani, as synonymous with *E. concentricum*. Later, in 1919, Castellani and Chalmers described *E. tropicale* as the species most frequently met with in Ceylon.

Symptoms. The invading organisms are presumably introduced through a breach of surface caused by a scratch or otherwise, and take root in the epidermis between the stratum corneum and rete. Manson and others, in the course of experimental infection in man, have been able to follow the evolution of the disease. After an incubation period of about ten days, the site of inoculation assumes a darker hue over a small circular area of the epidermis which

becomes slightly elevated by the multiplying fungus underneath it and soon gives way in the centre. This produces a ring with ragged edges of dry, curled tissue-paper-like, overlapping scales, more or less triangular in shape, attached at their bases to the periphery where they merge into the surrounding normal epidermis. This ring grows in circumference while the centre of newly regenerated epithelium goes through the same process and an inner ring is formed. According to different observers, from four to eight or ten concentric rings may be present in one system separated by apparently healthy epidermis. Repetition of the infection by scratching and auto-inoculation into other parts of the skin results in the pathognomonic appearance of complicated systems of concentric designs. Scratching, an important feature, and friction of clothing separates the scales which may attain considerable dimensions on such parts as the interscapular area which may be beyond the reach of the patient's nails. Pruritis is a distressing symptom and may induce secondary infections with subsequent enlargement of axillary and inguinal glands.

FIG. 87. Characteristic patterns in *tinea imbricata* infection brought into evidence by first loosening the scales by vigorous rubbing with gentian violet ointment, followed on the next day by a short bath (without rubbing) to remove the colour from the healthy skin spaces. The bases of insertion of the scales remain coloured by means of this technique. (After Figueroa and Conant)

Practically any area of the skin is liable to infection with the exception of the hairs. The scalp, scrotum and moist folds of the skin, as well as the palms and soles, are very seldom attacked. If, as occasionally happens, the nails are involved, they become greyish, thickened, rough, brittle and furrowed with deep cracks.

Tinea imbricata is regarded as contagious and usually attacks the natives who go about in a semi-nude state. While children under ten are rarely affected, no age seems to be immune from this disease

which runs a chronic course and shows no tendency to spontaneous cure.

Diagnosis. *E. concentricum* appears in the cleared scales as cylindric cells, 2·5–3μ in length, forming aclosely entangled mycelium of a greenish tint. The scales, from which cultures are rather difficult to get, are best disinfected in absolute alcohol for fifteen minutes and then put in a 4 per cent liquid glucose medium to start germination. A few days later uncontaminated pieces are next transferred to glucose slopes of the same strength. When successful, fair-sized growth is obtained in three or four weeks' time.

FIG. 88. *Endodermophyton concentricum.* Colony on 2 per cent Sabouraud glucose-agar. (Original)

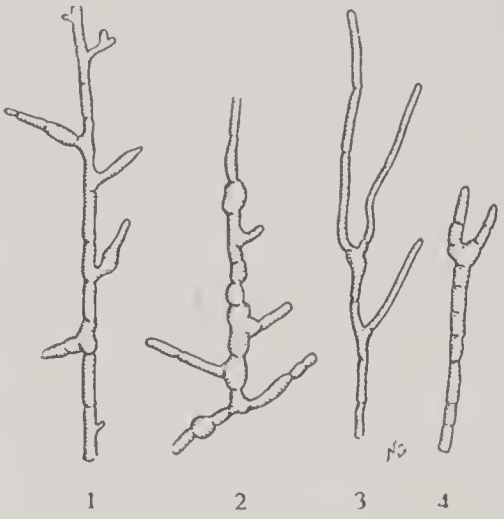

FIG. 89. *E. concentricum.* Cultural morphology. 1. lateral branching. 2. lateral branching and chlamydospores, 3. young hyphae, 4. arthrospores. (Original)

Colonies of *E. concentricum* crinkled or cerebriform, dirty white, becoming light amber or bright brown, with no velvet. Hyphae septate, 3–4·5μ in diameter, dichotomous, chlamydospores, 6–9μ, terminal, lateral, or occasionally intercalary. Cultures of *E. indicum* on 4 per cent glucose-agar slow of growth, powdery-white surface, with central knob or furrowed, central portion deep orange or lighter. Mycelial cells up to 5μ, spherical, becoming ovoid or cylindric. Cells become detached as thick-walled arthrospores with age. On the same medium *E. tropicale* grows abundantly, surface cerebriform or crinkled, light amber in colour, getting deeper with age, velvet slight or absent.

The clinical diagnosis is based upon the distribution, character, and peculiar pattern of the lesions, especially in freshly infected areas. The disease is easily differentiated from other dermatomycoses, and any doubt may be relieved by microscopical examination of scrapings as well as by the result of cultures.

Treatment. Nearly all the usual applications induce improvement or apparent cure which, however, does not last for more than a few weeks after discontinuing the treatment. Strong liniment of iodine, resorcin in compound tincture of benzoin, ℥ii to ℥i, or a 5 per cent chrysarobin ointment, are among the tried therapeutic agents. Plain weak tincture of iodine is also recommended, and chrysophanic acid (1 in 15 of vasline), according to Tribondeau, is claimed to be specific. A 5 per cent salicylic acid ointment has effected a cure in a very refractive case (Raymond, 1929).

A little friction applied to the diseased areas with frequent baths to which disinfectants may be added are useful adjuncts to treatment before applying the ointments. Against contagion, isolation of the patient, boiling the clothing and personal linen, and other hygienic measures are certainly essential if they can possibly be enforced.

CHAPTER IX

EPIDERMOPHYTOSIS—*continued*

Trichomycoses by Members of the Group Trichophytoneae

Popularly referred to as ringworm of the scalp, the most redoubtable amongst these mycoses is favus. Less serious infections are those due to invasion of the hairs by species other than the organism of favus, *Achorion schoenleini* and allied species.

Several classifications of these infections have been proposed by Sabouraud and others who based their views on clinical or mycological features, opposing each other's conclusions most vehemently and often reverting eventually to the original pioneer works of Sabouraud. He classified the parasites into mycological groups on cultural grounds, as well as according to their respective appearances *in situ*. The genera concerned have been shuffled and reshuffled on various occasions, and even the mycelial elements in or on the hair in the different types of infection are not of sharply defined modes of distribution. But, for all its drawbacks, Sabouraud's system is applicable, *faute de mieux*, which seems unattainable.

Sabouraud's System of Classification

1. Genus *Achorion*, and allied species, the saprophytic or cultural forms.

The parasites of favus in man and animals, as they occur in the infected hairs, filling up its interior in the form of thick and thin, straight and sinuous, long and short, more or less parallel mycelial filaments, sometimes dividing by tri- and tetratomy.

2. Genus *Microsporum* and allied genera and species, the saprophytic or cultural forms.

The parasites of microsporosis, easily recognizable as small arthrospores, 2–4μ in diameter, held together irregularly in a mosaic pattern by mutual pressure and encasing the infected hair at its base.

3. Genus *Trichophyton* and allied genera and species, the saprophytic or cultural forms.

The parasites of trichophytosis divisible into:

A. Endothrix type (*tondante* or shorn type), in which the hair is packed with parallel contiguous filaments composed of chains of arthrospores, medium-sized and of equal dimensions.

B. Ectothrix type, where the parasite occurs outside the hair in two alternative forms:

(*a*) Megaspores (of animal origin), of rare incidence, encasing the hair as filaments made up of spores 5–8μ in diameter.

(*b*) Microspores (microid of Sabouraud, also of animal origin), bearing a close resemblance to the *Microsporum* type, with spores 3–4μ in diameter, which occur in distinct longitudinal chains, contrasting with those of *Microsporum* in that they retain their pattern and are not disarranged into their component articles when disturbed under the microscope.

C. Neo-endothrix type in which, while most of the mycelium is restricted to the interior of the hair, a few hyphae are present outside it.

Since the mycelium invading a hair proceeds from without, it will spread, at least in the earlier stages of infection, on both sides of its sheath. The different types enumerated above really signify the predominant extent of the hyphae in relation to the hair, occurring mostly inside it in the endothrix type, and more abundantly externally in the ectothrix form.

Regardless of the foregoing divisions and subdivisions, the various genera, sub-genera and species concerned which have been erected or dropped into synonymy by botanically-minded mycologists, the subjects will be dealt with here under two broad headings. The first will be that of favus, the most serious infection in its course, sequelae and prognosis, and the other, of comparatively less consequence, under *tinea tonsurans* embracing microsporosis and trichophytosis. For further more specific differentiation, after the appearance of the organism has been noted in or on the hair, to determine the particular group it belongs to, recourse to cultivation of the diseased hair will be necessary. The treatment on all occasions is identical but the microscopical findings are of practical importance in its strict conduct and especially in so far as they determine the prognosis.

Favus

Historical. This infection was vaguely recognized and described by the Latins, Greeks and Arabs, including Celsi, Galen, Avicenna and Ali Abbas. Later, from the twelfth century onwards, French, Italian and English authors classified the various affections of the hairy scalp, including favus, among the conditions producing alopoecia, with a vague beginning of a differentiation of that infection as a separate entity. In 1837 Remak first reported on the favic crusts as being constituted of filaments of mould, and two years later Schoenlein demonstrated for the second time the vegetable nature of what he termed "the dry pustule of favus." In 1841 and the following years Gruby of Vienna, who emigrated to Paris during a wave of Jewish persecution in Austria, described, while unaware of Remak's and Schoenlein's discoveries, the parasite of favus *in situ* as well as other mycoses in a most comprehensive manner. Cultures of the organism, *Achorion schoenleini*, were attempted with some success in 1845 by Lebert and Remak to whom we owe the name, but it was Grawitz (1866) who first obtained pure cultures of the fungus. Since then Sabouraud's studies of this subject among others in the field of dermatomycoses rank foremost and remain to this day as standard and practically unassailable.

Aetiology and contagion. The following species have been isolated from favic lesions in man and animals:

Achorion schoenleini (Lebert, 1845) Remak, 1845; the cosmopolitan cause of favus in man.
A. muris (Gluge and d'Ukedem, 1857) Dodge, 1935; in mouse and hedgehog. (= *A. quinckeanum* Bodin, 1902).
A. gallinae (Megnin, 1881) Sabouraud, 1910; in turkey and fowl.
A. caninum (Costantin and Sabrazès, 1893) Dodge, 1935; in the dog.
A. gypseum Bodin, 1907; in the horse, rats, mice, cats, fowls and rarely in man.
A. serisei Cazalbou, 1913; in the horse.
A. cupressiforme Aoki, 1917; in man.
A. formoseum Hasegawa, 1927; in man, Formosa.
A. africana Dodge, 1935; causing a favoid condition in Bechuanaland, South Africa, among syphilitic natives.
Gymnoascus gypseus Nannizzi, 1927; in man, dog, cat and fowl.

The connection between favus in animals and in man, although a negligible quantity, yet has its importance. The incidence of infection is certainly higher in rural districts where man is in closer association with domestic animals. But at the same time human favus is almost always of human origin. This does not, however, overshadow the facts that in some cases there is reciprocal transmission

of the disease between man and animals, or that, at least in some instances, animal favus is experimentally inoculable into man.

Mice seem to be especially susceptible to favus. It occurs among them in epidemic proportions, attacking the head where godets cause perforation of the skull bones by pressure atrophy, and if the eyes or their neighbourhood are atttacked the animal dies from starvation following upon blindness, or of subsequent meningitis. The infection is probably transmitted from mice or rats to the cat and thence to the dog. Horses, rabbits, domestic birds and others also suffer.

Infection is possible at all ages in both sexes, but in practice the school-going age is the usual period of predisposition. It is rare in new-born infants and rarer still among adults or in old age, unless it be of chronic origin from younger days.

The rôle of trauma may be emphasized as a possible means for the introduction of favus into the body. Predisposing factors of hormonal, chemical or other nature probably operate to a large extent as is evidenced by the rarity of adult cases. Bad hygienic conditions, crowding in families and institutions, as well as low social status are distinctly favourable for the higher incidence of infection among the poorer classes.

Favus occurs sporadically, but hardly ever in epidemic form. Its powers of contagion are weak when contrasted with other mycoses of the hair, which fact can be readily understood if its characters *in situ* are studied and when its slow evolution is considered. In the hair, the mycelium is mostly enclosed within the cortex and the hair retains its strength barring the escape of hyphae. What fungus elements exist on the surface of the hair are firmly matted and held together by the crusts of overgrowing epidermal cells, sebum and débris, and consequently have a comparatively poor chance of being disseminated. Intimate promiscuity in poor families and in schools, although conducive to extension of favus from one infected member to others, does not necessarily result in general spread. A case on record is that of a married couple, one of whom was chronically infected and who, contrary to expectation and over long years, failed to transmit the infection to the other.

Invasion and evolution. The primary indication of infection appears on the epidermis of the scalp as an erythematous spot, slightly scaly, irregular in outline, growing in time to about a square centimetre in size, flat at first and later a little elevated. This is the first sign of invasion of the horny layer of the epidermis by the

fungus. It is on this red and scaly patch that there is produced in the thickness of the epidermis in the vicinity of a hair follicle a pseudopustule containing leucocytes. If ever examined, it will give off on puncture a tiny drop of pus. When this is removed the bottom of the pustule will be found to contain a tiny yellowish disc whose evolution would constitute the favic cup, *godet* or scutulum. This stage is of short duration and is seldom noted. As the scutulum grows exfoliation of the horny layer above it takes place, some of its superficial layers disintegrate, and it becomes umbilicate, assuming its characteristic cup-like shape, surrounds the hair in the thickness of the epidermis, and may attain from the size of a millet seed at the outset to a diameter of half a centimetre or more. A godet, as a rule crusty and dry, is composed of three zones: the innermost, around the hair, made up of matted hyphae broken up into arthrospores, a central one of mycelium and cells from the horny layer, while the outermost contains hyphae lying perpendicular to the surface of the scutulum, as well as a few infiltrating leucocytes. The epidermis on the extreme edge of the godet is of normal structure, but the underlying dermis is the seat of the usual fibrosis and infiltration which follows a process of chronic irritation. When a godet is lifted off the scalp it uncovers a smooth depression or a red and moist ulcerated surface.

Almost simultaneously with godet formation which is preparatory to invasion of the hair itself, hyphae reach the opening of a hair follicle, follow the epidermis which was initially attacked, and bend down with it into the follicle. The mycelium hugs the hair which, like the superficial layer of the epidermis, is keratinized. It soon penetrates it, deriving its nourishment from it, grows downwards and branches di-, tri- and tetrachotomously. The invasion, however, will not go beyond the point where the horny tissue ceases, that is at the neck of the follicular bulb, itself devoid of keratin, and from which new hair tissue is born. This continues to be formed and is infected as fast as it appears, while the bulb remains unaffected in its normal function. This accounts for the extreme chronicity of favus in some cases. Up to this stage of invasion the macroscopic character of the hair is unchanged. Visible signs of infection of its exposed part are only encountered about two or three months later when mycelium pushes upwards to above the level of the surface of the scalp.

Microscopic appearance of the favic hair. The interior of the hair along its long axis is found to be partially but not completely

occupied by parallel, straight or sinuous mycelial filaments 2–5μ in diameter, composed of long cells, about 12μ in length, sparsely ramified, and sometimes short arthrospores, while extra-pilary hyphae or arthrospores are occasionally met with. A collection of air bubbles, especially in the aerial portion of the hair, may also be noted. These are probably replacements by infiltration with air of the interior of desiccated, dead hyphae, a phenomenon which might explain the greyish discoloration of a favic hair.

FIG. 90. Mycelial filaments of parasite of favus arranged along the longitudinal axis of the infected hair. (Original)

Clinical features. The early appearances described above, namely the initial erythematous spots and the beginning of godet formation, only occasionally come under the medical man's notice except in the case of the more intelligent better class patients in whom such affections, however, are naturally rare. They occur more often amongst the poor, especially in rural districts. At this juncture, it is to be noted that godets are by no means a peculiarity of infection with favus, or that all favus cases develop godets. In other dermatophytic affections of the hair, false godets may be formed, but they are microscopic and transitory, disappearing as soon as the hair is parasitized. This is especially the case in animal infections.

When godets or flat crusts are apparent on the head, the evolution of the infection is recognized under different specific terms. Where the godets are discrete and small, the condition is known as *favus urceolaris*. When they partially run into each other, it is *favus scutiformis*, and if they constitute an agglomeration and lose their elementary character, they are of the *favus squarrosus* type. In some rarer cases with secondary microbic infection, an impetigenous

form with waxy yellow crusts that cover two or three lesions but no godets is liable to be mistaken for impetigo. Rarer still is the pityroid type suggesting pityriasis, psoriasis or dry eczema with lesions completely covered by grey adherent scales and easily detachable superficial ones. Underneath the crusts several pin-head godets may be discovered. The sulphur-yellow colour of favic godets is typical but often absent from admixture with dirt. A

FIG. 91. Favus of the scalp. (Original)

peculiar mousy odour can often be noticed about favic heads, a characteristic which is absent in other affections and almost pathognomonic.

The course of favus is very chronic, sometimes running from childhood or even infancy, the former being the most favourable age for infection, to very old age in untreated cases. With chronicity, folliculitis, crusts and secondary infections apparently stifle the hair follicles both mechanically and by scar formation until the bulbs eventually perish. Areas of alopoecia, in themselves results of healing, unfortunately at the expense of total loss of hairs in them,

PLATE I.

(*a*) Colony of *Trichophyton tonsurans*.

[*Water colour by N. Strekalovsky.*

(*b*) Colony of *Achorion schoenleini*.

[*Water colour by N. Strekalovsky.*

more or less extensively, are the final irreversible stages. At first isolated and separated by areas of active lesions or by healthy patches, later they become confluent. Favus alopoecia, unlike other forms, is characterized by scarring resembling that produced by burns. It is interesting to note here that body favus heals without scar formation. A characteristic, perhaps pathognomonic, feature of favus alopoecia is the occurrence in some cases of isolated tufts of two to eight hairs apparently issuing from one follicle.

FIG. 92. Favus alopoecia. (Original)

Apart from the appearances of crusts and godets, the macroscopic characters of the infected hair will have to be considered. It takes from two to three months for any changes in it to be recognizable, not until mycelium has grown upwards inside it to a level beyond the crusts on the scalp. The favic hair will then look dull, dry, grey or even white. In contradistinction to microsporic or trichophytic hairs, it is fairly tough and does not snap on attempted epilation with the forceps, since its substance is not totally replaced by hyphae.

Diagnosis. Before the formation of the godet, as well as in examples without godets, while the only evidence of infection discernible is the initial erythematous spot which represents the implantation of mycelium in the horny layer of the epidermis, diagnosis will usually remain unconfirmed pending progress of the

lesion. This early phase in the infection hardly ever comes under clinical notice. The discovery of mycelium in the hair as described above, the presence of godets, or arthrospores in the scales in earlier infections will leave no doubt as to the nature of the lesion. Naked eye changes in the hair will only be apparent from two to three months after the onset of the attack when the mycelium has grown downwards into the follicle, through the hair and up its shaft to a level beyond the surface of the scalp.

FIG. 93. Favus alopoecia. Growth of hairs in tufts of two or more apparently emerging from one single follicle, a phenomenon presumably brought about by cicatricial contraction of the skin of the scalp over destroyed hair follicles. Bare, smooth, scarred areas between the hairy parts. (Original)

The very early scaly stage may simulate dry eczema or the crusts of psoriasis. In the former there is usually a certain amount of oedema and burning or itching in a patch of erythema with ill-defined margins. In the latter other patches will be seen spreading over the forehead, neck and elsewhere, distinctive by their silvery colour. The fully formed crusts will have to be distinguished from those of impetigo, which are yellow or amber-coloured, or brown from admixture with blood and dirt, and from those of eczema. In this case the sequence of an erythematous stage with itching, a vesicular and bullous stage, a weeping stage, and finally the formation of crusts, is sufficient for its exclusion. The crusts of favus are usually fawn

in colour, dry, calcareous and friable. In cases of old standing, during the alopoecic stage, evidence of active favus may be discovered in other areas of the scalp but, if absent, other causes of alopoecia

FIG. 94. *Achorion schoenleini*. Giant colony and cup-like daughter colony on Sabouraud 2 per cent glucose-agar. (Original)

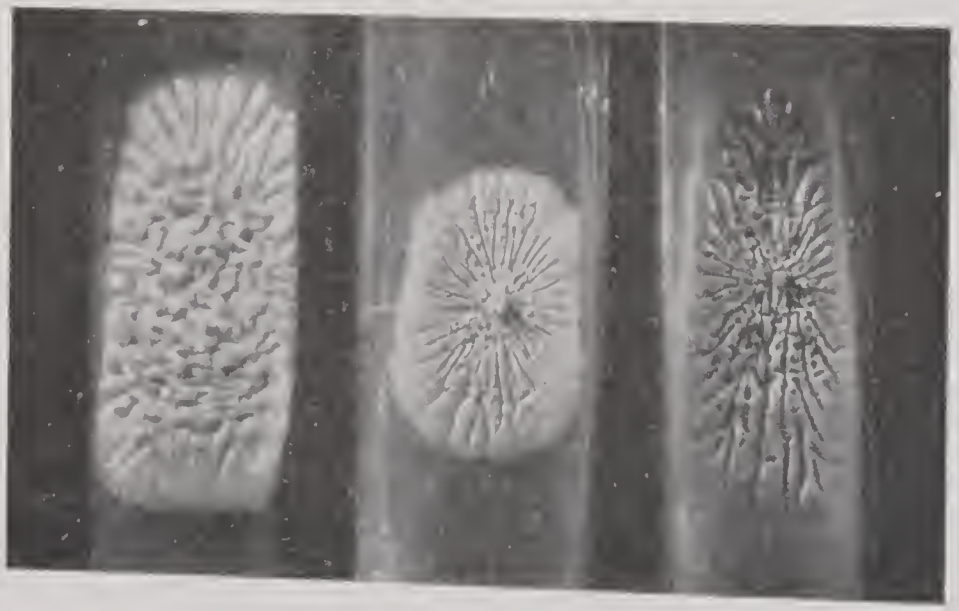

FIG. 95. Unusual comparatively flat, cerebriform, rugose and radially furrowed colonies of *A. schoenleini* on Sabouraud 2 per cent glusoce-agar. (Original)

should be sought. The surest method of diagnosis, however, is by means of the microscope. The greenish fluorescent character of infected hairs under Wood's light is very helpful, especially in the control of treatment. A secondarily infected, encrusted and dirty scalp of pediculosis may very well be mistaken for favus, kerion, etc. All kerions are not trichophytic or favic. The discovery of pediculi and their ova on the hairs will clear any doubt. Incidentally, a subject of favus is a very favourable prey to *Pediculus capitis*.

Cultures of *Achorion schoenleini* are yellowish-white, suggesting beeswax, cerebriform and heaped. Variants occur according to medium and locality. Arthrospores are the usual morphological constituents, but dichotomous club-like terminal swellings (*chandeliers faviques*), terminal nail-head chlamydospores (*clous faviques*) and chlamydospores may be obtained.

Tinea Tonsurans

History. Cazenave in 1840 gave under the name of *herpes tonsurans* the first comprehensive description of the mycotic affection of the scalp hairs. Since his work on favus, Gruby demonstrated the mycotic nature of *tinea tonsurans* and described the species *Microsporum audouini*. He enumerated in his account the following parasites:

1. That of what is now known as sycosis, composed of sporular elements between the hair and its follicle, the ectothrix type of trichophytosis.

2. The second in an infection which he called by a name then used for *alopoecia areata* but, according to his description, was apparently a *tinea tonsurans*. The parasite encased the hair with spores and penetrated it in the form of a few filaments.

3. A trichophyton endothrix restricted to the interior of the hair.

In 1845 Malmsten described a *Trichophyton* without growing it, which has since been named *Trichophyton tonsurans* Malmsten to denote the common cause of *tinea tonsurans* with the crater-like colony (*Trichophyton crateriforme* of Sabouraud). Following upon this, controversy started between Bazin and Gruby, the latter ascribing *M. audouini* wholly to *alopoecia areata*. Robin (1853), however, accepted Gruby's clinical picture of his species as that of *tinea tonsurans*, a view which was shared by most.

As for Gruby's trichophytosis of the hair, it remained unheeded for nearly half a century except for a paper by Aubert in 1876, in which appeared a perfect description of a hair twisted in the scales and infiltrated with spores, the trichophytic picture, as well as that

of a microsporic hair. He failed, however, to distinguish the two as totally distinct types.

In this field again Sabouraud and others finally ascertained the precise nature of these affections as we know them to-day.

Aetiology and contagion. In infections of the hair with species of the genera *Trichophyton* and *Microsporum* an animal source is to be suspected, the cat and the dog being the commonest reservoirs. Microsporosis is more common in boys than in girls, and predisposition is strongest in children of both sexes about the school-going age, but rarely after puberty when the processes are usually arrested spontaneously. The disposition of the parasites in connection with the affected hairs renders contagion, in contrast with favus, extremely rapid and almost inevitable. In trichophytosis and allied endothrix infections where the hair is ultimately packed with arthrospores, it is reduced at the expense of cortex and medulla to a mere delicate shell which soon gives and liberates spores. In microsporosis the fungus elements, because they surround the hair, are also liable, and from an earlier stage in the infection, to easy dislodgement and dissemination. Hardly a member of suitable age in a family, school etc., is likely to escape contracting infection from contact with a diseased subject, the common use of toilet articles, hats, etc., helping in the spread.

The following is a list of most of the species isolated from the diseased hairs, including localities, although these affections are cosmopolitan:

Trichophyton tonsurans Malmsten, 1845. Common in Western Europe.
T. sabouraudi Blanchard, 1896. Common in Europe.
T. flavum Bodin, 1902 (= *T. cerebriforme* Sabouraud, 1910).
T. fumatum Sabouraud, 1909. Common in North Italy and North Africa.
T. regulare Sabouraud, 1909. Common in Holland, reported from Austria and Tomsk, Siberia.
T. umbilicatum Sabouraud, 1910.
T. plicatile Sabouraud, 1910. Common in North Italy.
T. sulfureum Sabouraud, 1910. Common in England, Algeria and Australia.
T. soudanense Joyeux, 1912. Haute Guinée.
T. ochropyrraceum Muijs, 1924. Holland and Germany.
T. cineraceum Americo da Veiga, 1929. Brazil.
T. acutulum Americo da Veiga, 1929. Brazil.
T. bicolor Americo da Veiga, 1929. Brazil. Very contagious.
T. areolatum Negroni, 1929. Argentina.
Favotrichophyton violaceum (Sabouraud, 1902) Dodge, 1935. Common in Mediterranean countries.
F. discoides (Sabouraud, 1910) Neveu-Lemaire, 1921.
F. glabrum (Sabouraud, 1910) Dodge, 1935. Common in Algeria.
F. urenae (Ochoterena, 1924) Dodge, 1935. Mexico.

F. coccineum (Katoh, 1925) Dodge, 1935. Kyushu, Japan.
F. spadix (Katoh, 1925) Dodge, 1935. Loochoo Islands.
F. fuligineum (Ogata, 1929) Dodge, 1935. Japan.
F. abissinicum (Agostini, 1930) Dodge, 1935. Eritrea.
F. gourvili (Catanei, 1933) Dodge, 1935. Algeria.
F. floriforme (Beintema, 1934) Dodge, 1935. Holland.
F. avellaneum Dodge, 1935 (= *Trichophyton langeroni* Milochevitch, 1931).
Microsporum audouini Gruby, 1843. Common European species.
M. felineum Fox and Blaxall, 1896. Feline, common in England, Belgium and Northern Italy.
M. equinum (Delacroix and Bodin, 1896) Guéguen, 1904. Horse species, rare on man.
M. canis Bodin, 1904. Common on man but originally canine. Produces tinea tonsurans microsporica and herpes circinatus in children and adults.
M. villosum Minne, 1908. Belgium and Italy.
M. fulvum Uriburu, 1909. Argentina.
M. pubescens Sabouraud, 1910. Material from New York.
M. umbonatum Sabouraud, 1907. From Russia and Hungary.
M. tomentosum Pelagatti, 1910. Sardinia and Sicily.
M. flavescens Horta, 1912. Brazil.
M. lanuginosum Muijs, 1918. Holland.
M. ferrugineum Ota, 1921. Common in Japan and Manchuria.
M. japonicum Dohi and Kambayashi, 1921. Japan.
M. aureum Takeya, 1925. Japan.
M. orientale Carol, 1928. Japanese patient.
Atelothylax currii (Chalmers and Marshall, 1914) Ota and Langeron, 1923. From a Sudanese boy.

Occasionally species of *Aspergillus* and *Penicillium* may be isolated from the hairs, but they represent external saprophytes occurring as simple accidental deposits acting as mechanical irritants.

Invasion of the hair by a species of Microsporum and its evolution. A small erythematous spot is the first sign to be noticed and represents the inital attack on, and the reaction of the epidermis of the scalp. Circular in outline, with the edges slightly redder than the centre, its appearance follows in a matter of a few days the implantation of the fungus elements in the form of sinuous mycelium, 1–3μ in diameter. Very soon, however, when a hair in the vicinity is being involved, it disappears rather suddenly. The mycelium now insinuates itself downwards into the hair follicle, between the follicular epidermis and the hair, multiplying as it does so, and eventually forming a cone-shaped mass of fragments with its base upwards. The hair projects from it as its perpendicular axis. The fragments are about 14μ in length and 6μ in diameter, and already they include a few spore-like elements. At a level about the middle of the root of the hair some bifurcating mycelium, about 2–3μ in diameter, penetrates the hair subcuticularly downwards, finally

gaining the interior of the medulla, but in a scantier amount. Some of these, growing towards the surface and escaping through breaks in the cortex, may contribute some of the spores. More hyphae of similar size form a network in contact with and a little adherent to the epidermis of the follicular walls. By dichotomy outside the hair, the mycelial elements end by constituting the characteristic sheath of spores which by mutual apposition assume the typical mosaic pattern of this form of infection, and not the more regular arrangement suggesting a continuous chain as seen in trichophytosis.

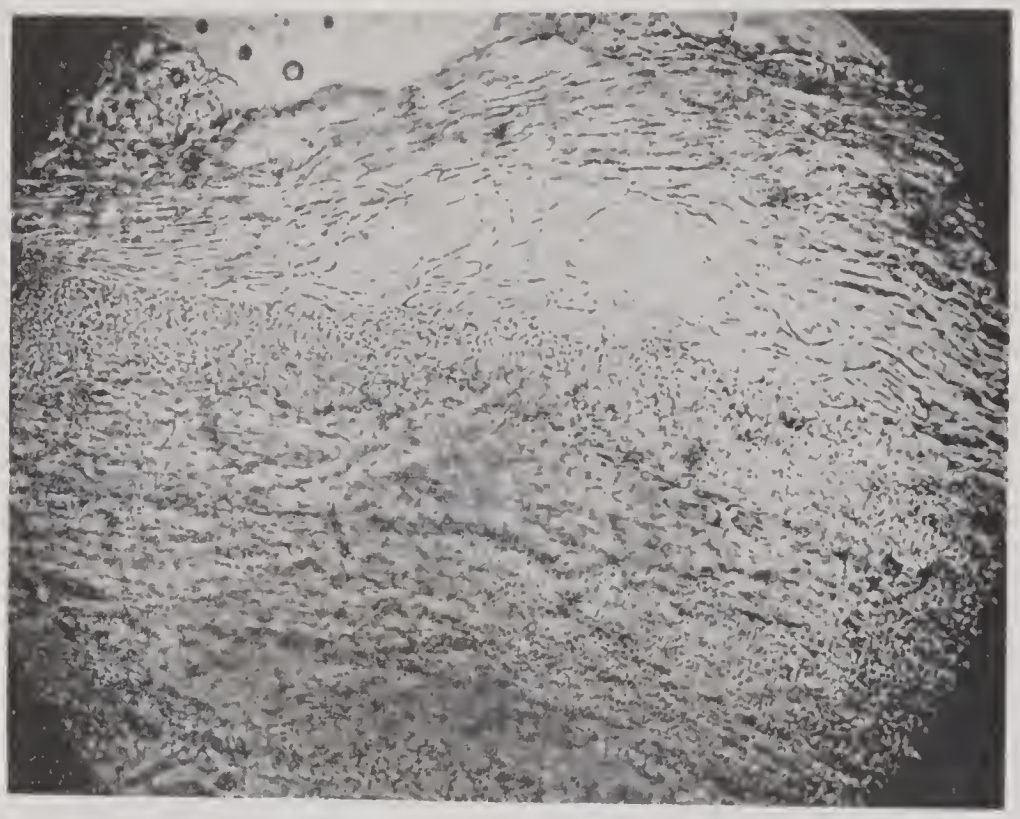

FIG. 96. Microscopic hair with a sheath of spores surrounded by epidermal scales, sebum and foreign particles. *Microsporum canis* infection. (Original)

Microscopic appearance of a microsporic hair. In cleared specimens of microsporosis of human origin spore-like bodies are seen to surround the hair in a more or less complete manner, according to the stage of evolution. The spores are 2–3μ in diameter, with a double wall and rendered polyhedral by mutual pressure which gives the well-known mosaic picture. This sheath of spores extends about 2 mm. within the follicle, gradually getting thinner towards the root on which only a few scattered groups of spores may be present. Scanty, septate, and fine intrapilary filaments but no spores are usually present. In infections with *Microsporum*

of animal origin, the difference lies in the larger size of the intrapilary hyphae.

FIG. 97. Microsporosis of the hair. Microscopic appearance of infected hair. (Original) (Drawing by N. Strekalovsky)

Symptoms and course in microsporic infection of the hair. The initial lesion is a small erythematous circular spot which in a few days loses its hyperaemia and is seen no more. This stage seldom

FIG. 98. Microsporosis. Sheath of spores surrounding affected hair. (Original)

comes under the notice of the medical man. Soon, however, the area becomes covered with grey scales, and signs of infection appear on the implicated hair which eventually becomes encased in a greyish sheath representing the spores for about 2–3 mm. from the follicular orifice.

PLATE II.

Colony of *Microsporum canis*.

[*Water colour by N. Strekalovsky.*

It is beyond this level that the hair snaps off. The contiguity of the exposed spores to healthy hairs causes widening of an infected

FIG. 99. Hairs infected by *Microsporum canis*. Sheath of spores and scales appearing white against surrounding normal black hairs as reproduced on the black background in microphotograph. They show black against a white background. (Original)

area which may attain 6 cm. in diameter, and in which the hairs are all infected. They become greyish-white in colour, easy to epilate,

FIG. 100. Microsporosis. (Original)

and are embedded in a mixture of grey scales and dirt. Auto-inoculation may implicate remoter areas of the scalp through the

agency of a mechanically detached broken hair, and the number of lesions is thus multiplied. Some of these may become confluent, but the spread is rarely so extensive as to include too large a proportion of the whole scalp.

In some instances the infecting strain may, for some obscure reason, be weak, or else the patient may possess a quality of resistance, and spread of the process is arrested. Such factors operating, the

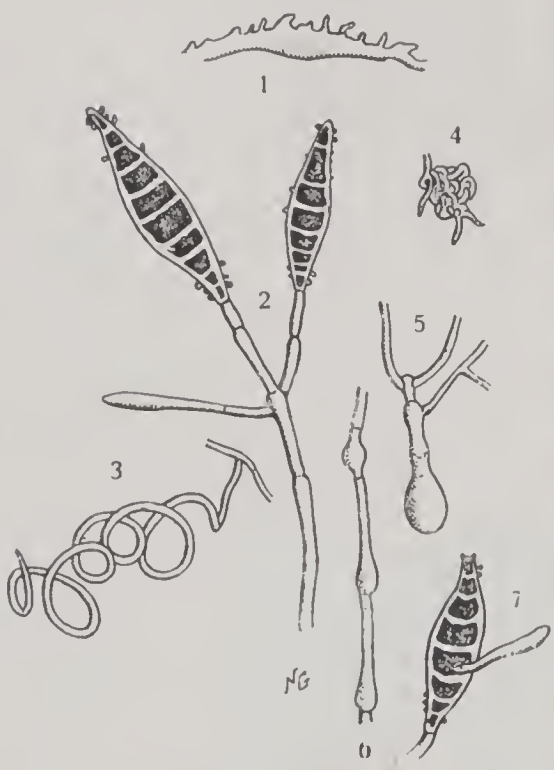

FIG. 101. *Microsporum canis*. Cultural morphology. 1. pectinate body, 2. closterospores (*fuseaux*), 3. spiral (*vrille*), 4. nodular body, 5. chlamydospore, 6. chlamydospore and racket mycelium, 7. germination of closterospore. (Original)

FIG. 102. A *Trichophyton*-infected hair *in situ*. Section reveals it charged with spores and surrounded on the surface of the scalp by heaped epidermal scales. Section misses the deeper levels of the root, which escapes infection. (Original)

diseased hairs fall spontaneously or are easily epilated together with their bulbs, and new downy hairs, which later grow to normality, begin to push their way on the alopoecic areas produced. This desirable possibility may take place a few months or a few years from the onset of infection, or it may be the outcome of the as yet mysterious influences brought about at the advent of puberty. Eyelashes and eyebrows are seldom affected.

Invasion of a hair by a member of Trichophyton or one of its allies and its evolution. As in microsporosis, the initial lesion

is epidermal until the fungus elements encounter a follicular orifice. Insinuation proceeds downwards into it, and there they assume an irregular arrangement suggestive of the mosaic of microsporosis.

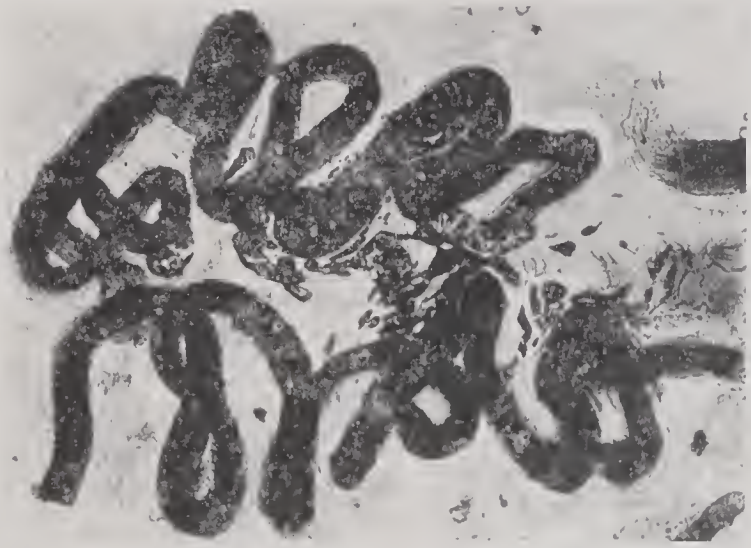

FIG. 103. *Favotrichophyton violaceum* infection of the hair. Spirally twisted and embedded in scales. (Original)

The mycelium insinuates itself subcuticularly and this penetration takes place as a rule in the upper third or middle of the root of the hair. As soon as the fungus gains access into the medulla, its

FIG. 104. *F. violaceum* infection of the hair. Cortex burst and spores discharged. (Original)

mycelium divides dichotomously and its two branches proceed closely together downwards. Repetition of this process eventually produces such an abundance of parallel filaments composed of fragments or "spores" as to entirely fill up the hair, which becomes

irregularly swollen, cracked, serpigenous, and reduced to a mere fragile, incomplete shell. This description explains the pure endothrix type of infection. In a neo-endothrix invasion there is, over

FIG. 105. *F. violaceum* infection of hair, which is a mere thin envelope containing masses of arthrospores bursting through in places. (Original)

and above the intrapilary "spores," a certain amount of multiplication of fungus elements which takes place around the hair. Whilst this is the rule, there may still exist some hairs on the same scalp which show a typically pure endothrix appearance. At the same time the

FIG. 106. Hair infected with *F. violaceum.* Cortex and medulla practically wholly replaced by chains of arthrospores arranged longitudinally in the hair. (Original)

extrapilary elements are a common feature in any type of invasion in its earlier stage, an understandable condition, since the attack proceeds from without. The duration of the initial picture in these cases is, however, very short and does not persist long enough to be seen in all of them. In this connection it is to be noted that in all

trichophytic infection of animal origin, the hair retains always, or at least for some time, the characters of the early days of invasion. As for the ectothrix type of infection, the hyphal fragments enshcath the hair without penetrating it, the picture often encountered in trichophytic invasions of the beard.

Microscopic appearance of trichophytic hairs.

(*a*) *Pure endothrix-infected hairs.* Such hairs will be seen to enclose parallel chains of fungus elements, "spores," which are almost straight and rarely branching. If ramified, the division is always dicho-

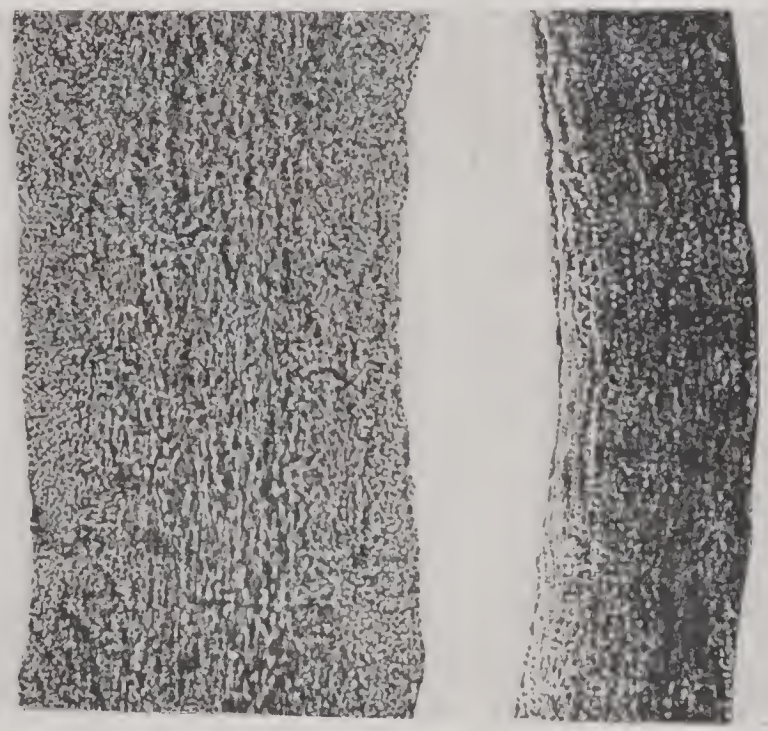

FIG. 107. Contrasting trichophytosis and microsporosis of the hair. Left: *M. canis* infection, a sheath of spores surrounding the hair. Right: *F. violaceum* infection, spores in linear longitudinal parallel disposition filling up and replacing the hair substance. (Original)

tomous and in a downward direction. The "spores" are spherical, oval or cylindrical, and vary between 3 and 8μ in diameter.

(*b*) *Neo-endothrix-infected hairs.* Here the mycelium will be mostly within the hair, but a certain proportion is found persisting around it from the earlier stages of invasion.

(*c*) *Ectothrix-infected hairs.* In these the "spores" exclusively surround the hair as in microsporosis without attaining the medulla. They may be of two grades of sizes differentiated into a microid type, about 4μ in diameter, and a megaspore type, from 5 to 8μ in diameter.

Symptoms and course in trichophytic infections. An erythematous spot, similar to that which first appears in microsporosis, ushers in the infection in trichophytosis. It is, however, more transient and less likely to be noticed, and is quickly replaced by a crust of scales, about 1 mm. in thickness, yellowish in colour and entangling both infected and healthy hairs. Contrary to what is seen in microsporosis, the lesions, when they multiply, are smaller in size, more numerous and discrete, and the number of infected hairs in each is comparatively small and they have to be carefully sought.

Two pictures, depending upon the aetiological agent, may be

FIG. 108. Trichophytosis of the scalp hairs. (Original)

presented by the hair. In infections with *Trichophyton sabouraudi* (=*T. acuminatum*) and its satellites, the diseased hair snaps off flush with the scalp at the follicular orifice which, therefore, appears as a black spot. When the infecting agent is *Trichophyton tonsurans* (=*T. crateriforme*), or one of its allies, the implicated hair is found folded upon itself and embedded in the scales, and is usually about 5 mm. in length. In the first type, as opposed to the second, the number of infected hairs in a given lesion is, as a rule, greater. In a few instances, short shorn hairs, yellowish and straight, about

2–3 mm. in length, may be seen, and except for the absence of a spore sheath they suggest microsporosis. In *F. violaceum* infection the hairs may retain their normal length, break off at the follicles and lie loose amongst the normal hairs against which they appear grey.

Secondary infection is a common occurrence when a member of the ectothrix microid group is the parasite. The degree may vary from a slight erythema around the follicular orifice of an invaded hair, to a further stage of distinct folliculitis, and up to a red, elevated and ulcerated, more or less extensive area similar to a kerion. Another type may be met with in which the lesions become impetigenized. Pyogenic infection, although a complication, yet has a salutory effect on the duration of the fungus infection. While uncomplicated lesions may run a chronic course for years, the pyogenic cases end in cure by elimination of the fungus in periods in inverse ratio to the activity of the suppurative process. About seven weeks would see a severe case through to a desirable termination, which ordinarily is only attained in about as many months if the fungus has a span of life uninhibited by secondary infection. Warty overgrowth of the epidermis is occasionally seen at and around a group of diseased hairs and is brought about by long-sustained irritation.

Fig. 109. Hairs infected with *F. violaceum*. They were lying loose among normal black hairs, against which they stood out white, as reproduced against black background of picture. Scaling almost absent in this particular case. (Original)

Although newly growing hairs are weak and appear at a slow rate, alopoecic areas are comparatively rare sequelae unless scarring follows suppuration, a possibility in the severer varieties as well as in cases on whom too strong fungicides are carelessly employed.

Diagnosis. The clinical features of both microsporosis and trichophytosis of the scalp as enumerated above should be helpful. The naked eye characters of the involved hairs are distinctive.

The stumpy shorn hairs of microsporosis, and those broken off flush with the scalp or folded up in the crusts in trichophytic infections are often self-evident on careful examination, if necessary with the aid of a magnifying lens. But microscopic examination of the diseased hairs when found, and cultures, are really essential and will easily clinch the diagnosis and determine the specific nature of the infection. Nothing short of demonstrable mycelium or spores about

FIG. 110. Multiple warts in a case of *F. violaceum* infection of the scalp hairs. (Original)

the hair can ever justify a diagnosis of favus or *tinea tonsurans*. The one has to be differentiated from the other and from similar conditions. From an evidential standpoint, clinical features alone can prove very misleading. A neglected, secondarily infected and encrusted scalp in pediculosis for instance may easily pass for favus, or the two conditions may co-exist. Areas of seborrhoea have often been mistaken for *tinea tonsurans* but are distinguishable by their generally abundant branny desquamation. The scales are easily detached and lie loose among the hairs and fall off on to the back of the neck and shoulders. Patches of pityriasis may also co-exist

PLATE III.

Colony of *Favotrichophyton violaceum*.

[*Water colour by N. Strekalovsky.*

on forehead, neck or face. The condition is much more extensive than is the case with *tinea tonsurans*. Other infections are rather unlikely possibilities in differential diagnosis. The question of house pets should also be enquired into, especially in microsporosis.

The Eyelashes

The eyelashes are rarely affected either primarily or secondarily to tinea of the eyelids or face. The lesions may occasionally be sycosiform co-existing with infections of the beard or moustache.

The Eyebrows

These are much less commonly affected. A few saprophytic species, *Aspergillus fumigatus*, *A. niger*, *Penicillium* sp. and *Mucor racemosus* have been isolated from simple, slightly desquamating and pruritic lesions which showed a few spores with the scales, while the hairs themselves were not involved.

Examination and Culture of Hairs

An epilation forceps with rounded ends, and a small, sharp-edged, diamond-shaped or spear-like knife, about 1 cm. long (Fig. 86), are the requisite instruments for picking diseased hairs from the scalp. In the case of favus, the forceps is used, and sharp traction is applied to the hairs in the direction of their natural growth, thus removing them easily and without undue pain. More than one hair from different infected areas where scales abound, or at the borders of an alopoecic patch, are selected, for normal hairs occur side by side with diseased ones. If present, a godet is carefully undermined and lifted up by means of the knife, and the hair running through its centre is epilated, allowing hair and godet to be removed together. Hairs infected with *tinea tonsurans* parasites are sought where they lie coiled up, buried in or even loose among the scales. Occasionally, because of their short-shorn character, the hairs can only be detected through a hand-lens after careful scrutiny. They require delicate manoeuvring for their removal, and if hidden, the scales removed for the purpose should be teased on a slide with a white background. This procedure will often expose unsuspected cases. A helpful sign of hairs infected with the parasites of *tinea tonsurans* is that they appear white against a black background, and vice versa. Even an apparently normal looking scalp, with perhaps what might be

diagnosed clinically as simple dandruff, should never be neglected. Extremely short diseased hairs may be discovered only after long and extensive search. The tip of the knife is then used for removing them after a slight shaving movement to the scales with the blade.

The hairs are examined microscopically, cleared under the cover-slip either in the classical 10–30 per cent potassium hydroxide solution, or in chloral-lactophenol. The clearing agent may be heated on the small jet of the Bunsen burner and immediately withdrawn on ebullition. This serves to drive away any air entangled in the scales and hairs. The disadvantage of heating the preparation is apparent in the case of favic hairs in which the air inside some mycelial filaments is lost, together with the refractile power which would render it more detectable. It is, therefore, best to dispense with the process of heating in examining for favus. A cheaper and more available medium for examination is plain water, which serves the same end in the same way, especially to experienced eyes.

Before making cultures, the hairs and scales should be kept between two slides for about a week to dry them and destroy any contaminating bacteria. Washing them in 80 per cent or absolute alcohol for a few minutes is a quicker way to obtain the same result. The diseased hairs are cut up on a slide, employing the knife and a dissecting needle for support, into 2 or 3 mm. lengths, which are then inoculated on three or four slopes, about three pieces per tube, and incubated at 25 degrees C. It is essential to bear in mind while cutting up the diseased hairs, particularly those suspected as favic, that the pieces are apt to fly off and be lost, apart from the risk of contagion. Applying the blade very obliquely to the hair and the exertion of firm pressure will obviate that. Microsporic and trichophytic hairs are usually soft and are less likely to fly about on being cut. The needle in Fig. 86 is used with advantage in inoculation, and in transfers, especially in tearing off a piece of hard and adherent colony. It is made of hard chrome-nickel wire, bent as shown, and its end hammered flat into a cutting tip.

For macroscopic characters of colonies for diagnosis, 4 per cent Sabouraud glucose-agar is used. In this connection, some of the dermatophytes, when grown on such rich media, are liable to undergo in time what is known as pleomorphism. This is a tendency of the culture, irrespective of the species, to complete transformation into a sterile white cottony colony, an irreversible process even after animal inoculation, ending in total loss of the initial characteristic colony. To avoid this, Sabouraud's conservation medium is em-

ployed. It supplies the best chance for maintaining a dermatophyte unchanged for the longest possible period through several transfers.

When microscopic features of a species are needed for accurate determination, natural media are necessary, and include grains of barley, wheat or rice, or an agar-polysaccharide like dextrin or soluble starch. A further advantage of these media is that they do not favour pleomorphism.

A valuable aid to diagnosis in favus and in ringworm infections of the scalp hairs is the fluorescent property which they, as well as their scales, exhibit when exposed in a dark room to ultra-violet rays of wave-lengths between 3,600 and 3,300 Ångström units. To obtain these particular rays the light of a mercury-vapour lamp is filtered through a sheet of Wood's glass (deep violet nickel-oxide glass). These rays are invisible to the naked eye as they are beyond the visible spectrum. The glass screens the visible spectrum and only allows 70 per cent of the ultra-violet rays through. Advantage is taken of this method in detecting persistent infected hairs, otherwise hard to locate, during treatment and even before in early or puzzling cases. It is to be remembered, however, that yellow vaseline also fluoresces brilliantly, and every trace of ointment should be removed from the scalp with ether before the test is undertaken. In microsporosis, the hair fluoresces a bright greenish yellow which is less bright in favus, while trichophytic hairs give a dull bluish grey fluorescence.

Trichophyton tonsurans colonies on glucose-agar are white, velvety, crateriform, becoming powdery and occasionally buff-coloured, with a small button in the centre. Aleurospores, often sessile, lateral and in thyrses and clavate hyphal tips are seen together with small chlamydospores.

T. sabouraudi Blanchard (= *T. acuminatum* Bodin). On glucose-agar, colony at first a small hemispheric mass with several long, slender coremia which show less with age. Colour changes gradually to powdery white, cream-white, then becomes brownish, sometimes with a violet tint. Older colony becomes a flattened cone with radiating furrows and a thin flat border. Lateral aleurospores in irregular thyrses, and small chlamydospores are seen.

F. violaceum. On glucose-agar, colony violet, rounded, often with a little button in the centre, surface shiny with a few irregular radial folds. In older cultures, short velvet, white, covering colony except the centre. Chlamydospores, arthrospores and aleurospores are seen.

Microsporum audouini. On glucose-agar, colony a small velvety disc with a tiny point in the centre, white or light greyish with a few radial furrows. With age these disappear as the growth enlarges and concentric circles of long and short velvet form. Hyphae straight or curved with clavate tips. Aleurospores, 2–4μ, chlamydospores terminal or intercalary, closterospores (*fuseaux*) rare, spirals (*vrilles*) on special media.

M. canis Bodin, 1904. Colony similar to *M. audouini* at first but more

velvety and grows more rapidly with a glabrous and powdery central area, then forming a white loosely woven zone about the centre, which later becomes umbilicate and often sprayed with little drops of water of condensation. The periphery of immersed rays produces a short greyish velvet which is yellowish on Sabouraud's glucose-agar. Closterospores abundant, several-celled, with distinct asperities at their free ends. Intercalary chlamydospores, occasional aleurospores and pectinate hyphae are seen.

Animal Inoculation for Pathogenicity

Animal inoculation is carried out on guinea pigs. The hair of the animal is shaved or cut very short on the back between its shoulder blades, and an emulsion of the culture is rubbed into the skin, which may be previously very lightly scarified. Another method is to inoculate the parasite into the dermis on a thin sharp needle. Diseased hairs can be detected in about a fortnight after inoculation and spontaneous cure takes place generally in a month's time. One inoculation confers immunity.

Treatment of Favus and Ringworm of the Scalp

In treating with this subject, favus, the most intractable of hair affections, only need be considered, for what is employed against it is equally applicable, in fact more effective, in curing trichophytosis as well as microsporosis.

The fungous elements in the three conditions, present as they are inside the hair in favus and trichophytosis, and mostly surrounding it in microsporosis, render the application of a fungicide on the infected hair an abortive attempt at cure. In microsporosis the spores around the hair may seem accessible, but wherever they happen, they are endowed with a remarkable power of resistance to destruction by chemical or physical means. The problem resolves itself into ridding the patient of his infected hairs, parasite and all, while taking measures at the same time to guard against reinfection of newly pushing hairs from stray diseased ones that may have escaped.

The truth of the above principle was arrived at by the ancients, perhaps not scientifically, but it proved at least justifiable through experience, and epilation was practised then as it is now as the method of treatment with the greatest promise of success. With progressive ideas and evolution of science, the means to that end underwent a change from the "tar cap," *capellus piceus*, and the epilatory forceps to thallium acetate and the X-rays.

A tar cap is a bonnet made of strong linen on which is spread a pasty mixture of black tar with resinous turpentine or some caustic substance, the recipe varying in composition in different hands, but tar plays the essential part. The cap is applied firmly to the scalp to be removed suddenly and without anaesthesia some days later when the tar hardens, pulling off with it all or the majority of the hairs. The process may have to be repeated if the epilation is incomplete. Eventually, the bare scalp is treated with an ointment with some disinfectant as a basis. This method, though cruel, is effective, but is only practised in out-of-the-way corners of the globe where primitive conditions still prevail. Depilation by forceps, it is needless to say, is both tedious and far from thorough.

Thallium acetate. The depilatory properties of thallium were only ascertained towards the end of the nineteenth century, and its acetate salt was used about the same time for the night sweats of tuberculosis, gonorrhoeal arthritis, tabetic visceral pains, diarrhoeas, etc., but it fell into disfavour owing to its toxicity. Sabouraud (1913) employed it in hypertrichosis in women as well as in ringworm infections of the scalp with perfect results, but once again the disquieting symptoms—cardiac, vascular, renal and secretory—to which it gave rise precluded taking full advantage of its depilatory action for a time.

Further research, however, by Buschke in Germany, and by Cicero in Mexico in large-scale treatment of microsporosis in children, in this case by means of the protoxide of thallium, which was considered more stable, revived interest in the drug. The net results of work on the subject, undertaken mainly in Europe, brought to light practical theories concerning its pharmacology and settled its therapeutic dosage within safely effective limits.

The fact that only some hairs fall after the administration of thallium—the hairs of the scalp and the tips of the eyebrows, while the eyelashes and the deeper portions of the eyebrows as well as the pubic hairs remain immune—led to the formulation of theories in explanation of this selectivity on the part of the drug. One of these is based on the probability that hairs whose follicles receive direct sympathetic innervation are the only ones to be affected. Another is that thallium increases the excitability of the sympathetic ganglia and blocks nutritive reflexes. From these and more attempts at interpretation of findings during animal experiments coupled with clinical experience, there emerged a workable technique for thallium therapy.

Tolerance for thallium acetate is highest among very young children, from one to four years of age, and the drug is especially suitable in their treatment owing to the difficulty of keeping a child of that age immobilized sufficiently long under the X-rays. After the age of four, but only till puberty, thallium may be, and has consistently been employed by the Russians, but this amounts to taking unnecessary risks and should be avoided whenever possible.

7 and 9 mg. per kilogramme of body-weight may be given, and represent respectively the minimum effective dose when weak patients are dealt with, and the safe maximum as suggested by certain authors. A maximum dose of 0·3 gm. is laid down and should never be exceeded even in adults or when the body-weight justifies it. The margin between the toxic and effective doses of thallium is so very narrow, but an average of 8·5 mg. would meet most requirements. The salt in solution, freshly prepared in distilled water (5 c.c. for 0·1 gm. of the salt) is given in one lot on an empty stomach and may be flavoured with some sugar or fruit-syrup. It is essential to ensure full dosage by well draining the glass. Thallium acetate deteriorates on exposure to light, losing its depilatory properties and becoming more toxic.

In about a week or two, the hairs which do not fall off of their own accord are ready to be removed and must be helped off by means of a hair-brush or a fine tooth-comb. Slight traction draws them out painlessly in tufts and complete alopoecia is obtained about the eighteenth day. It is advisable to have the hairs cut fairly short before the commencement of treatment so that any stumps of the fragile diseased hairs will not escape notice and can be picked out with a forceps. Occasionally, it happens that some hairs are spared over forehead, temples and nape, together with scattered islands on the crown. These are often in a healthy state, but should not be left on that account as they are usually accompanied by persistent infected stumps and must be extracted with forceps or better by adhesive strapping followed by sudden withdrawal.

Failure of thallium acetate to bring about the desired full alopoecia may indicate a repetition of the dose, but this ought not to be undertaken earlier than two or three months after the first administration of the drug as it has a cumulative property and may cause toxic symptoms.

New hairs, at first downy and later of a normal thickness, start to grow in three or four weeks' time. In order to avoid reinfection, the scalp has to be treated from the very beginning, during the fall

of hairs and right through to the end until the newly growing hairs are fully established. Epilation, when complete, is a cure in itself, but in favus with godets, disinfectant applications and fungicides are necessary. All the same, they do no harm and should be employed as a matter of routine. The scalp is washed every morning with soap and warm water and then painted with weak tincture of iodine, 2 per cent diluted 10 times in 60 per cent alcohol, and a 10 per cent sulphur ointment applied every night with gentle rubbing. Another effective method combines oil of cade with yellow oxide of mercury. It is well to advise the wearing of a linen cap which well covers the head, especially at night, and which must be changed frequently and thoroughly sterilized by boiling.

Among the toxic symptoms sometimes encountered during thallium acetate treatment the following may be noted:

Abdominal pains which may be accompanied by vomiting, erythema, cutaneous ecchymoses and tachycardia, albuminuria, excessive salivation, neuritis and muscular and articular pains.

These untoward occurrences are more often than not the outcome of excessive dosage or impurities in the drug, but for safe practice, the urine should be systematically examined for albumin as evidence of impaired kidneys, and careful consideration of the individual's general health is necessary, especially where there exists a discrepancy between age and weight. It is well to refrain from employing thallium in unsuitable cases in whom the use of X-rays instead may have to be entertained. An association of both thallium acetate, reduced to two-thirds of the normal dose, and shortened exposure to X-rays also gives very good results in such patients.

Following upon the administration of thallium acetate, the child must be watched so that if any toxic symptoms arise they can be met promptly.

X-rays. Recourse to X-rays for depilation, if a plant is available and if in capable hands, is the best course, especially in older children who usually begin to develop idiosyncrasy to thallium after the age of five.

Prior to exposure, the hairs must be clipped very short and applications of pyrogallic acid, iodine or other ointments should be stopped so that the penetration of the rays may not be hindered.

Sabouraud and Noiré in Paris perfected a technique for exposure to X-rays for the purpose of depilation compatible with a maximum of effectiveness and safety because the rays, unless applied by an experienced operator or if prolonged, may bring about an irreversible

alopoecia or at least X-ray dermatitis. They use small discs of paper covered with platino-cyanide of barium, the Sabouraud-Noiré pastilles, which under normal conditions are of a bright yellow colour with the property of losing their fluorescence and changing to a brown tint when in the path of the rays. By experiment, Sabouraud and Noiré fixed the requisite dosage for depilation as that sufficient to produce this change in colour in the pastilles when interposed half-way between the ampoule and the child's head. The duration of exposure may also be measured with an ionometer previously set by means of a pastille.

As used in the Hôpital Saint-Louis and the école Lailler, the X-ray apparatus consists of the ampoule which is enclosed in a large sleeve of sheet iron lined with ebonite as an insulation lantern for the protection of the operator. To an orifice in the centre of this sleeve the Noiré localizer in which the pastille is put is attached.

According to Sabouraud's method, five fields with centres 11 cm. apart are mapped out on the head, and for the rays to be effective those of every centre of irradiation must be perpendicular to neighbouring centres, which arrangement is rendered possible by means of the localizer. After the ampoule is centred (Kienboeck-Adamson method) the rays are allowed to act on one field at a time at an exact distance of 17 cm. between anticathode and scalp; meanwhile the rest of the head is protected by sheet lead. Depilation must include the whole head, which can be dealt with in five consecutive sittings in the course of one day.

The hairs begin to fall or can be plucked off easily and painlessly about a fortnight after exposure, and new ones show two months later. It is interesting to note that they are found to contain viable fungi, which proves that the rays, as is also the case with thallium, possess no fungicidal action. Hairs which still persist one month after exposure may be again subjected to half the dose.

After depilation, however produced, detection of persistent infected hairs is possible by virtue of their fluorescent character under a Wood light, and they ought to be pulled off individually as they will compromise the success of the treatment. There seems to be a growing tendency to resort to manual depilation under an ultra-violet light, thus avoiding the possible complications arising after the administration of thallium.

The same treatment with washing and fungicides mentioned in connection with thallium depilation should be practised from the beginning.

PLATE IV.

Colony of *Epidermophyton persicolor*.

[*Water colour by N. Strekalovsky.*

Among the symptoms that occur in children after exposure to X-rays, headache, photophobia, and in some cases persistent vomiting may be cited.

Institution treatment. The ideal practice in the treatment of ringworm or favus of the scalp is the isolation of the children in special centres where strict routine is followed and sure results are to be expected while rendering contagion a remote possibility in schools and homes. Their usefulness is such that, very often, one month from the institution of treatment, the child can return home, and cure ought to be obtainable in two months.

Local applications. Without having recourse to depilation these are not without their value in a certain number of cases and may be given a trial. Whatever fungicide is used for the purpose, the hairs should be clipped short and kept so and the scalp thoroughly washed with soap and warm water every morning. White precipitate ointment (10 per cent) is rubbed in nightly and on alternate mornings. On the intervening mornings all visible patches are painted with 5 per cent aqueous solution of mercurochrome. Painting the patches with weak tincture of iodine, with a drop of croton oil carefully applied because of its highly irritating effect, or with an ointment incorporating bismuth violet are among the therapeutic measures employed. Control of progress by means of a Wood light or by frequent microscopic examination is, however, essential with such topical agents.

Kerion of Celsus

Preceding, simultaneous with or following upon a fungus invasion, a pyogenic infection of the follicles of the area involved may take place. The term, used mostly in connection with the complicating lesions on the scalp, may also be employed, be it to a lesser degree, in ringworm cases of the glabrous skin and in sycosis. The folliculitis, when it becomes multiple and extensive, together with the mycosis, constitute the condition.

Aetiology. Children represent the majority of sufferers, but adults contribute a fair proportion to the whole. Members of the groups *Trichophyton*, *Microsporum* and *Achorion* are the offending organisms. The following is a list of species incriminated in kerions:

Ectotrichophyton mentagrophytes (Robin, 1853) Castellani and Chalmers, 1919. Affects the glabrous skin and the beard.

E. felineum (Blanchard, 1896) Castellani and Chalmers, 1919. Produced a vesicular inflammation of the glabrous skin and kerions; in pruritis ani, in which instance the mycosis was probably a secondary invasion.
E. lacticolour (Sabouraud, 1910) Castellani and Chalmers, 1919. Producing multiple kerions of the beard.
E. farinulentum (Sabouraud, 1910) Castellani and Chalmers, 1919. Producing kerions of the scalp and glabrous skin in children and adults.
E. nakamurae Dodge, 1935. From kerion of the scalp, Japan.
Favotrichophyton ochraceum (Sabouraud, 1908) Neveu-Lemaire, 1921.
F. discoides (Sabouraud, 1910) Neveu-Lemaire, 1921. From kerion in sycosis.
F. flavivirens (Americo da Veiga, 1929) Dodge, 1935.
F. luxurians (Brault and Viguier, 1914) Neveu-Lemaire, 1921.
Microsporum felineum Fox and Blaxall, 1896.
M. japonicum Dohi and Kambayashi, 1921.
Achorion schoenleini (Lebert, 1845) Remak, 1845.
A. gypseum Bodin, 1907.
A. violaceum Bloch, 1911.

FIG. 111. A severe case of kerion. (Original)

Symptoms and course. Contiguous folliculitis will form slightly elevated and convex, infiltrated, red, oval plaques of various sizes according to confluence or discretion. The surface of a plaque is covered with multiple pustulettes from which dead, loose or semi-detached hairs and pus can be expressed on slight pressure. Underneath the kerion, a layer of pus and abscesses eventually forms, and the separate or confluent plaques drop in time. Healing follows by

scar formation with a more or less irreparable alopoecia. Spontaneous cure, though rare, may take place in a few months' time.

Diagnosis. In the early stages of its development a kerion is recognized by the co-existence of a mycotic infection as well as by an accompanying folliculitis. When it is fully formed, its appearance together with microscopic evidence of mycelial elements in connection with the hairs in the area involved will establish the diagnosis as distinct from other pyogenic infections of the scalp or beard. One kerion-like condition may occur in pediculosis capitis among poor, dirty and unintelligent patients when the scalp is completely neglected. In such cases the pediculi and their ova will be in glaring evidence.

Treatment. Kerion, being in most cases a pyogenic folliculitis complicating favus or ringworm of the scalp or glabrous skin, attention is primarily directed towards treatment of the bacterial infection. Softening lotions, starch poultices or oiled lint are first used to detach the crusts. Generally speaking, the plan recommended for sycosis is effective here. Sulphanilamide ointment gives very good results in combatting the pyogenic invasion. The concomitant ringworm or favus is attended to on the usual lines although, as it often happens, the fungus dies spontaneously in the purulent medium.

Tinea Barbae
Sycosis of Mycotic Origin

Tinea barbae is usually an occupational infection occurring mostly in subjects in close association with domestic animals, especially the horse. The following species have been isolated from the lesions:

Ectotrichophyton mentagrophytes (Robin, 1853) Castellani and Chalmers, 1919; from the glabrous skin and beard in man, and from the horse. The species belongs to the endo-ectothrix group.

E. radioplicatum (Fischer, 1913) Dodge, 1935; from the glabrous skin and beard of a coachman.

Megatrichophyton roseum (Bodin, 1902) Dodge, 1935; from the epidermis and hair follicles of the beard. Commonly spread through barbers' shops. Endemic in the greater part of Europe and in North England.

Favotrichophyton epilans (Mégnin, 1890) Dodge, 1935; occurs on calves in Normandy, very contagious to man, producing *tinea barbae*, as well as to the horse.

F. violaceum (Sabouraud ap. Bodin, 1902) Dodge, 1935.

F. discoides (Sabouraud, 1910) Neveu-Lemaire, 1921.

Trichophyton flavum Bodin, 1902 (= *T. cerebriforme* Sabouraud, 1910); not yet isolated from animals.
T. plicatile Sabouraud, 1910; common in Central Europe.
T. fuscum Dodge, 1935 (= *T. fuscum sulcatum* Neuber, 1925); occurring in youths' newly growing beards.
Achorion gypseum Bodin, 1907.
Microsporum xanthodes Fischer, 1918; Germany.
Aleurisma guillermondi Grigorakis, 1927; from two brothers in Lyon.
Trichosporum ovoides Behrend, 1890; Germany.
Debaryomyces nadsoni Guillermond and Péju, 1921.

Simple accidental deposits in the form of species of *Aspergillus* and *Penicillium* may occur on the hairs of the beard and moustache.

Symptoms and course. Sycosis is generally an intradermic suppurative condition of the pilosebaceous follicles, and is either primary or preceded by a dry type of infection which, while it lasts, corresponds to a trichophytosis. The sites of election are the beard and moustache areas, but the nasal hairs are not immune. The fungus induces an inflammation of the follicle, and the lesion soon evolves into a pustule with accompanying tumefaction or even a warty change giving it a nodular appearance. Its situation, as a rule at varying depths of the dermis, may occasionally be very superficial, just subjacent to a thin covering of epidermis, or actually hypodermic. The hair projects from the centre of the lesion and pus may be squeezed out of the more superficial nodules with or without the hair. The pustules may be discrete, or by successive eruptions and merging of contiguous foci, the pathological process may involve fairly wide areas which become elevated and firm. Dried pus around confluent lesions often lends them an impetigenous character. Being an endo-ectothrix type of infection, a depilated hair, especially at the periphery of a patch, will have spores or mycelium around it. The lesions are as a rule benign and heal spontaneously, the more superficial they are, the sooner the cure, which may not be accomplished for some months in the case of deeper ones. Scarring is a common sequel.

FIG. 112. *Sycosis barbae mycotica.* Early infection of the under surface of the chin and on the shaved anterior aspect of the neck and sides of moustache. (Original)

Diagnosis. The presence of white or grey scales and circinate lesions at the onset may render early diagnosis possible. Later on,

microscopic examination of the hairs in an involved area will reveal fungus elements around them, while cultures supply confirmatory evidence. The hairs to be examined should be selected from the edge of the lesion. Spores, 5–6μ in diameter, in more or less long chains can be detected in the contents of the vesicles. In the sheath that surrounds the hair follicle, mycelium and unequal chains of spores 2–11μ in diameter may be found.

FIG. 113. *Ectotrichophyton mentagrophytes* infection of the hair in *tinea barbae*. Sheath of spores surrounds the hair. (Original)

Ectotrichophyton mentagrophytes colonies on Sabouraud glucose-agar have a round elevated centre with powdery rays, then umbilicate with lanceolate rays covered with white powder where they reach the surface of the medium. Closterospores, 3–5-celled, few chlamydospores, aleurospores in thyrses, and spirals are formed.

Sycosis of fungous origin might be mistaken for an impetigenized eczema or acne. Neither, however, will be confined to the hairy regions of the face, and the latter condition is not covered with crusts. Ecthyma of the trunk and limbs is of rare occurrence on the face; its lesions extend deep into the corium, the pustules and scabs are surrounded by a distinctly red areola, and there is accompanying

slight induration. Pustular syphilides may be recognized by other syphilitic manifestations. Finally, coccogenic sycosis, an obstinate infection, usually staphylococcal (*S. aureus*), is a fairly common infection and very apt to be confounded with mycotic sycosis. Its pustules, however, are smaller and more uniform and the infiltration is more deeply seated. Furthermore, the hairs are more easily and painlessly pulled off in *tinea barbae*.

Treatment. The hairs of the beard or moustache should be kept short by clipping them with scissors, and they are not to be shaved. Frequent bathing with hot boracic acid or other antiseptic lotion

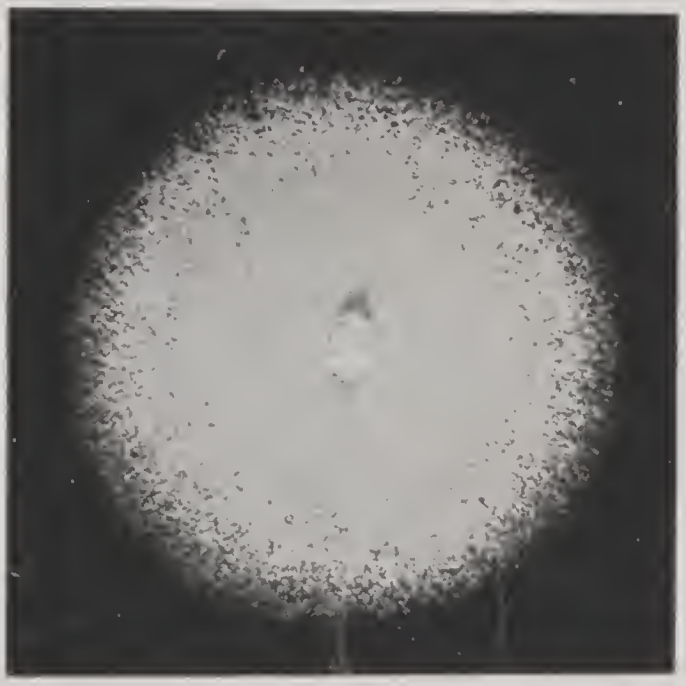

FIG. 114. *E. mentagrophytes.* Colony on Sabouraud glucose-agar. (After N. F. Conant *et al.*)

is recommended to soften and detach formed crusts. If acutely inflamed, the lesions are treated first with zinc sulphate in calamine lotion (gr. iii to 1 oz.). As many infected hairs as possible should be depilated with forceps.

For fungicidal therapy, perchloride of mercury (1 in 1,000 of 60 per cent alcohol), mercuric nitrate, sulphur or resorcin ointments may be used twice daily. Before each application the beard is washed with soap and hot water. Weak tincture of iodine (1 in 5 of 70 per cent alcohol) occasionally proves enough to bring about a cure. In obstinate cases intravenous Lugol's iodine injections may be tried (1 c.c. in 5 c.c. bidistilled boiled water). This dose is increased daily by 1 c.c. until 5 c.c. of iodine in 15 c.c. of water are

injected. This maximum dose may be continued for a fortnight. Other refractive infections have yielded to one or two exposures to X-rays, acting in the same manner as in the treatment of ringworm of the scalp hairs. Local fungicidal applications should, in such cases, be insisted upon directly after the exposures, while the hairs are falling and for a period after apparent cure to guard against recurrence.

Trichophytic Granuloma of Majocchi

The predilection of members of the group *Trichophytoneae* for dead keratin, the horny layer of the epidermis, the hairs and nails, is on rare occasions deviated from and the fungus will attack the dermis and hypodermis of the scalp. Majocchi (1883) was the first to give this exceptional behaviour a clinical status.

Symptoms and course. The initial stage takes the form of a herpetiform scaly lesion of short duration followed by alopoecia of the part. A rosy erythematous change in the skin of the area involved follows, and one or more papules develop. Growing sometimes to the size of a bean, they become nodules which are fairly hard at first, softening later and assuming a dusky-red hue. If superficial, the lesions may assume a warty character. The erector muscles of the hairs, the sweat and sebaceous glands may all become implicated. The evolution of a granuloma is slow and proceeds with a fungus-infected hair as a nucleus, surrounded by a zone of giant cells and an outer one of mono- and polymorphonuclear cells, endothelial and plasma cells, as well as a few supporting strands of vascular fibrous tissue. The surface of the growth may be smooth, fissured or cauliflower-like. The course is usually very chronic and is accompanied by acute inflammation unless there is a secondary infection when, on softening and breaking down, the nodules will give off blood, pus and blood-stained serum.

Diagnosis. The mode of evolution of the granuloma, taken in conjunction with discovery of mycosis in a hair in the growth, will determine the diagnosis to the exclusion of other similar affections.

Treatment. This is necessarily and primarily directed at the original infection. At the same time X-rays are effective in bringing about a cure.

Onychomycosis

Aetiology. Mycotic infection of the nails may be primary, or secondary by extension from neighbouring or remote lesions, favus being the commonest in this case. Not only members of the group

Trichophytoneae are responsible, but yeasts, yeast-like fungi and others have been isolated and are included in the following:

Achorion schoenleini (Lebert, 1845) Remak, 1845, in comparatively few cases.
Microsporum audouini Gruby, 1843.
Favotrichophyton coccineum (Katoh, 1925) Dodge, 1935.
F. violaceum (Sabouraud, 1902) Dodge, 1935.
Trichophyton tonsurans Malmsten, 1845.
T. sabouraudi Blanchard, 1896.
T. flavum Bodin, 1902 (= *T. cerebriforme*, Sabouraud, 1910).
T. plicatile Sabouraud, 1910.
Epidermophyton floccosum (Harz, 1871) Langeron and Milochevitch, 1930.
E. rubrum Castellani, 1910.
E. persicolor (Sabouraud, 1910) Dodge, 1935.
E. interdigitale (Priestley, 1917) MacCarthy, 1925.
E. pedis (Ota, 1922) Dodge, 1935.
E. cerebriforme Dodge, 1935.
Ectotrichophyton otae Dodge, 1935 (= *Sabouraudites ruber* var. *blanche* Hashimoto, Irizawa and Ota, 1930).
Syringospora albicans (Robin, 1853) Dodge, 1935.
Castellania unguim (Bourgeois, 1915) Dodge, 1935.
Myctoruloides unguis (Weill and Gaudin, 1919) Langeron and Talice, 1932.
Debaryomyces gruetzii Ota, 1924.
Mycocandida onychophila (Pollacci and Nannizzi, 1926) Langeron and Talice, 1932.
Hanseniospora guilliermondi Pijper, 1928.
Parendomyces periungualis (Niño, 1930) Dodge, 1935.
Schizoblastoporion gracile (Zach, 1933) Dodge, 1935.
S. globosum (Zach, 1933) Dodge, 1935.
Parasaccharomyces oosporoides (Zach, 1933) Dodge, 1935.
Aspergillus unguis (Weill and Gaudin, 1919) Dodge, 1935.
A. gratioti Sartory, 1920.
A. jeanselmei Ota, 1923.
A. diplocystis (Sartory *et al.*, 1930) Dodge, 1935.
Scopulariopsis brevicaulis var. hominis Brumpt and Langeron, 1910.
S. cinereus Weill and Gaudin, 1919.
S. aureus Sartory, 1922.
S. minimus Sartory *et al.*, 1930.
Sporotrichum schencki (Hektoen and Perkins, 1900) Matruchot, 1910.
Coniosporium onychophilum Agostini, 1931.
Hyalopus onychophilus (Vuillemin, 1931) Aschieri, 1932.
Cephalosporium spinosum Negroni, 1933.

It may be noted here that these species in their variety are the products of positive cultures in a comparatively small percentage of the cases. Cultivation of infected fragments or scrapings of nails is seldom attended with success. Onychomycosis is a rare occurrence among children under twelve years, and young females seem to be more susceptible than males. Familial contagion is possible. Trophic, neuro-trophic and endocrine, acquired or congenital factors may predispose to infection and should be borne in mind during treatment.

Symptoms. The description given by Sabouraud (1910) of the lesions due to Trichophytons serves the general purpose here. The

FIG. 115. Onychomycosis. Broken and fissured nails. *Epidermophyton persicolor* infection. (Original)

initial change is usually situated on one of the lateral borders of the nail and appears as an opaque yellowish-white spot of irregular

FIG. 116. Epidermophytic onychomycosis with extension to epidermis. Heaped-up scales and fungus elements lifting up the nails from their beds. *E. floccosum* infection. (Original)

margins, characterized by Lespinasse as dendritic. According as to whether the surface layer of the nail is attacked or not, two types of the progress of the lesion are possible. In the latter case

the deeper layer becomes spongy, greatly increased in thickness and friable at its free margin and is mainly composed of heaped epidermal cells. This may, in some instances, eventually lead to separation of the pathological mass under the external layer, which consequently assumes a convex claw-like appearance in one or two diameters over an empty space in the distal half of the nail, a condition known as onychogryposis. It may also be fissured longitudinally, opaque, dirty white or yellowish in colour. When the surface layer happens to be the seat of primary involvement, it is by degrees fissured, softened, brittle, atrophied and finally eaten away in its distal half

FIG. 117. Favus onychomycosis. Furrows, ridges and pits. (Original)

or further (onychorrhexis). The process goes on without inflammation for years on end, in the course of which other nails of one or both hands become implicated.

In the case of favus, which attacks the nails in comparatively few cases and is as a rule secondary to favus of the hair or body, the mycelium is restricted to the horny layer and is never found in the epidermal cells below the horny substance. The external layer of the nail becomes uniformly thickened, or only hypertrophied in small spots, of yellowish colour, composed of layers of scales and hyphae and, to the naked eye, suggestive of psoriasis. Eventually, after cracking (onychoschizia) of its external layer, the nail becomes friable and deformed.

Although the above-mentioned pathological changes in mycoses

of the nails are more or less typical, there is really no particular rule, and some or all the features of the infection may exist in a given case.

Diagnosis. Although the discovery of the fungus in the diseased tissue is essential before a case is diagnosed as onychomycosis, the parasite is not always demonstrable in scrapings from the surface of the nail or among the overgrown spongy mass of epidermal cells under it. Comparatively few attempts at culture have been rewarded with positive results. Psoriasis may be excluded by the

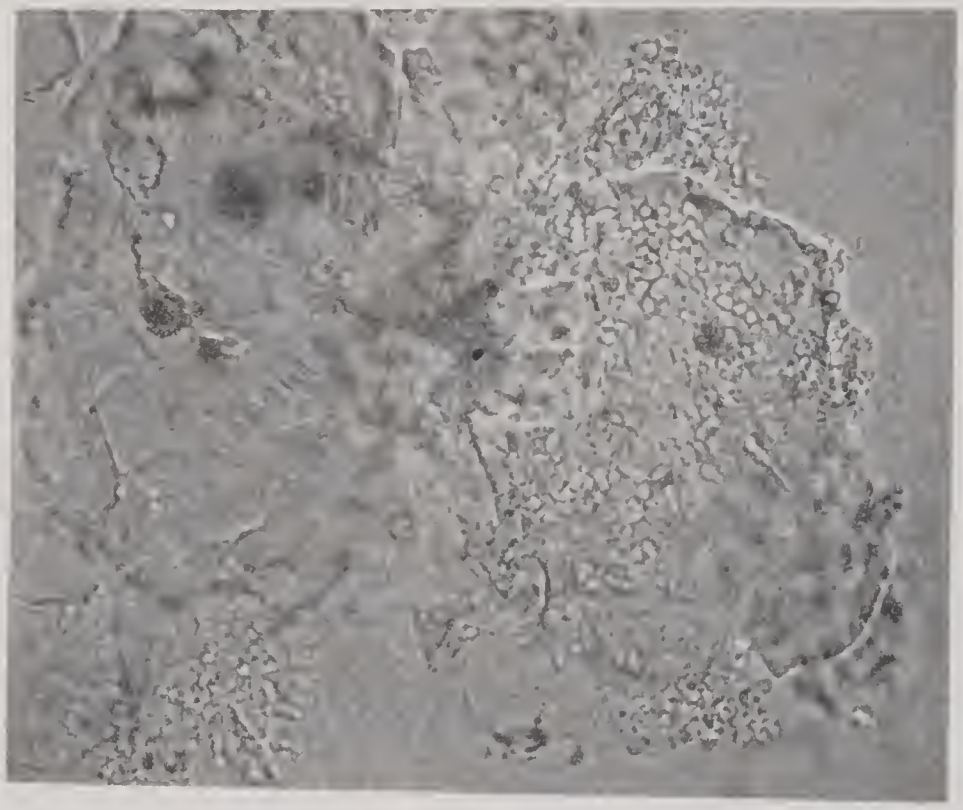

FIG. 118. Onychomycosis. Scrapings of infected nail revealing fungus elements and débris. (Original)

absence of its typical lesions elsewhere on the body. Eczema of the nail is another point in differential diagnosis and may simulate a psoriasis infection. Syphilitic and tuberculous manifestations in the nail should also be considered.

Treatment. It is of importance that the remedial agent employed should remain for as long as possible in direct contact with the infected nail in a state of solution for it to produce the maximum effect. This is best attained by means of warm baths of some fungicide. The finger-tips are immersed in it for 15 minutes at a time twice or more often daily. Potassium permanganate (1 in 1,000 or in 2,000) has given the author very satisfactory results.

New healthy nail tissue begins to grow underneath the diseased and discoloured parts, which are shed in the bath or may be lifted off in fragments. This treatment should be religiously and persistently carried out for about two months and continued for some time after apparent cure without flagging. Sabouraud has advised the use of Gram's iodine solution.

Surgical avulsion of the diseased nail has been suggested, but apart from being impracticable in most instances, it lays bare a delicate epidermal layer of cells which are likely to be infected anew by stray mycelial elements. To avoid such a possibility the exposed nail-bed has to be guarded with antiseptics or fungicides from the beginning. Radium, X-ray therapy and high-frequency current have also proved of value in some cases, but recurrences are frequent.

Application of sulphanilamide or chrysarobin ointment every night under the nail is a useful adjunct to the permanganate bath treatment. To be effective, the space between the nail and its bed should be regularly cleared of dirt and remains of ointment and epidermal cells before every bath or application of ointment. Rose sticks with bevelled ends such as are used in manicure serve this purpose well. Scraping of the nail surface may also be performed occasionally to get rid of as much infected material as possible. To ensure thorough action of a fungicide long contact is essential and may be accomplished by the wearing of cotton gloves over the hands at night after application of the ointment. Lugol's iodine solution may also be used as often as convenient during the day to wet the hands and nails, and is left to dry in the air. Administration of vitamin B_1 induces better response to treatment.

Phytids

This general term comprises the more specific ones, epidermophytids, trichophytids, microsporids and favids, according to the organism incriminated in the original infection, and is intended to designate occasionally occurring spontaneous lesions at situations far removed from a primary mycotic focus and apparently unconnected with it. They may take the form of exanthematous eruptions, erythematous, scarlatiniform or eczematoid. *Lichen trichophyticus* expresses their apparent character, which is that of subcutaneous follicular nodules that may go on to a stage of vesiculation, and sometimes to pustule formation. They appear mostly on the lower half of the trunk, abdomen and back in small or large crops.

Lesions, more or less resembling the original mycotic patch, are also liable to develop in the same fashion and are more in keeping than the exanthematous ones with fungus infection. Traumatized areas are often the starting points of phytids whose eruption seems to be favoured by the devitalized state of the part following the injury. Phytids are apparently sterile as they yield no evidence of fungous elements and may be explained as corresponding to the allergic reactions of subjects previously sensitized by inoculations of trichophytins, etc., devoid of mycotic toxins.

CHAPTER X

EPIDERMOPHYTOSIS—*continued*

Pigmented and Depigmented Dermatomycoses
Pityriasis Versicolor

Definition. A mycotic affection of the skin producing finely desquamating patches variously coloured with different degrees of pigmentation.

History, aetiology and geographical distribution. The fungous origin of this disease was first recognized by Eichstedt in 1846, and the causative organism, *Malassezia furfur* (Robin, 1853) Baillon, 1889, was described and named from its morphology in the infected skin. Attempts to obtain it in culture from the hyphae and spores in the scales are attended with indifferent results; the growth is exceedingly slow and the colonies attain at best very minute dimensions, and die quickly in spite of frequent subculturing. The affection is cosmopolitan and bears no relation to climatic or geographical factors.

Symptoms. The sites of election are about the sternum and between the shoulder-blades, the so-called sweat-gutters, but, generally speaking, it is mostly found on the anterior surface of the chest and lower part of the neck just above the clavicles and over the deltoids. Other localities are seldom affected, and the hands and feet are always immune. This apparent immunity or rarity in these situations is conceivably due to frequent washing and constant shedding of the epidermis where the fungus exists. It is consequently being continuously rubbed off, if it happens to be present, and cannot therefore establish itself. Although the classical site of election is the trunk, German writers record it as of common occurrence in the genital regions of prostitutes (Mulzer), and on the pubic area of women in general (Plaut). Keller claims to have discovered foci of the disease on the scalp by fluorescent examination. Peripheral extension and merging of the patches may end by involving practically the entire surface of the body until very few spots of normally-coloured skin are left. In some cases the initial patch may stay limited to one spot without any variation in size,

shape or colour, or may reform on the original site after apparent cure by treatment.

The lesion generally begins around follicular orifices as round or irregular, circumscribed or confluent spots of various sizes, as small as a lentil or as large as a half a crown piece, or even larger. They are as a rule smooth, especially on the cleaner patients, but may be slightly rugose, and rarely a little elevated above the surface of the

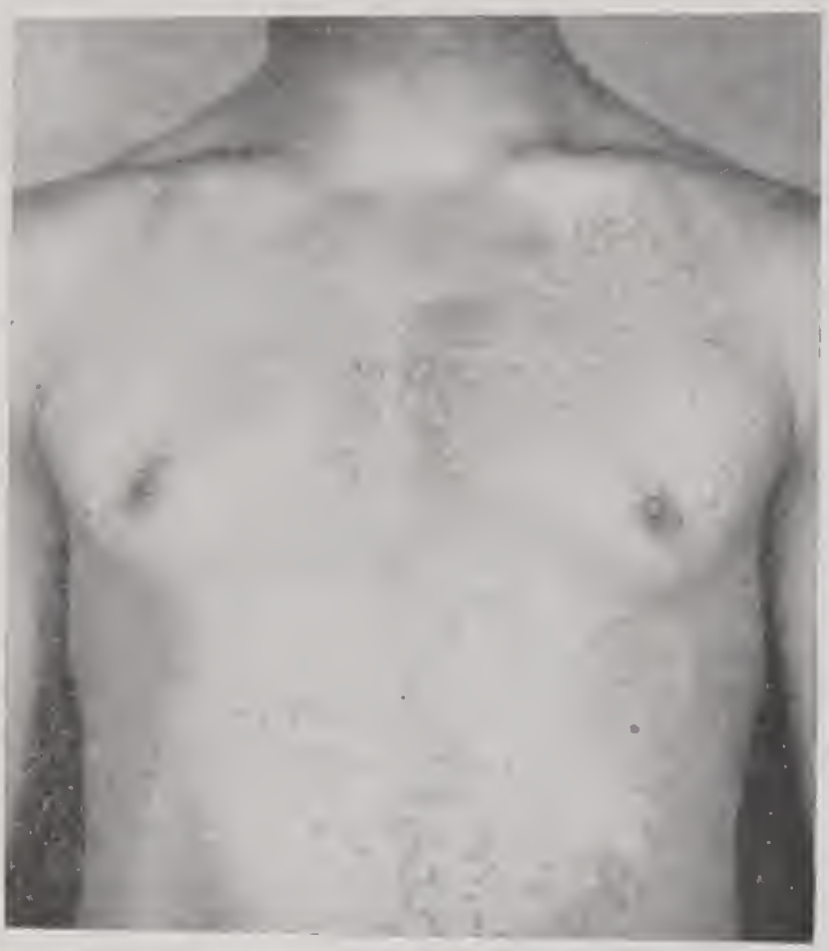

FIG. 119. *Pityriasis versicolor.* Neck, chest and abdomen. (Original)

surrounding normal skin. On closer scrutiny, they may be found covered in more chronic cases with fine furfuraceous or bran-like scaling which can be detached with a nail as thin lamellae of epidermis, the "*coup d'ongle* of Besnier," a pathognomonic sign.

The coloration varies from yellow to different shades of brown or black, but *café au lait* describes the colour more commonly observed. Occasionally rose to red spots are seen in new infections where there may be a slight amount of inflammation, and hyperpigmentation on the borders of the patches, similar to what takes

place in vitiligo, is sometimes present, generally on the sternum. In some of the more chronic cases leucodermic patches may be discovered. The name "versicolor" given to the disease by Willan implies the behaviour of the spots, which change colour from time to time, a phenomenon explained as being due to a state of increased irritability of the blood vessels below the fungus, the superficial circulation reacting to mechanical or psychological stimuli and producing the variations.

No subjective symptoms or constitutional disturbances can be

FIG. 120. *Pityriasis versicolor.* Chest and neck (anterior aspects). (Original)

traced to the disease, except for some pruritis, occasionally aggravated by perspiration in the rarer acute cases.

Young adults of both sexes constitute the bulk of sufferers and the infection has a tendency towards spontaneous cure in elderly patients. Among the predisposing causes, rightly or wrongly assumed as such, are malnutrition, intestinal stasis, tuberculosis, etc. Excessive perspiration, hot weather and the wearing of irritating woollen or tight-fitting underclothing, if they do not favour, at least strengthen and prolong the course of the disease once it is contracted.

Contagion is very weak, and judging by the slow and poor growth of the organism in culture, this may be understandable. The means of transmission is unknown.

Diagnosis. The appearance of the patches, their distribution and the "*coup d'ongle* sign of Besnier" should render diagnosis easy. This can be confirmed by discovering the characteristic fungus microscopically in the epidermis. In the cleared scales the parasite can be easily seen in the superficial corneous layer of the epidermis as short, irregular, unbranched hyphae, about 3μ in diameter, and as very refractive spores, spherical or ovoid, 3–8μ in diameter, occasionally striated with spiral striae formed by budding

FIG. 121. *Pityriasis versicolor*. Mycelium and spores in the scraped epidermal scales. (Original)

which often occurs in some of them, and they are generally collected in clusters.

Streaks on glycerol agar produce free glistening yellowish growth. In a week white droplets form on the surface, enlarge to about 2 mm. in diameter and become crateriform. Kambayashi (1932) described growth in liquid media as follows: Spores ovoid or elongated ovoid, 5–6 × 4μ, occasionally nearly spherical. Hyphae short, pointed or rounded at extremities, 2–4 × 2·6μ in diameter, straight or partially curved. In older cultures hyphae longer, abundantly ramified, abjointing ends of short lateral branches on a poorly differentiated conidiophore. Conidia sometimes in short chains of 2–3 cells, 3–5–6 × 4μ. On Sabouraud media growth is very slow, a growth the size of a rice-grain requiring 9 months. Colony whitish-yellow and slightly verrucose. This size is reached in 20 days from first sub-culture. Colonies yellowish-white, moist, with grooved and knotted

surfaces. With age the yellow colour changes respectively to grey, yellow, and finally brown, and the moist surface of the earlier stages becomes drier and chalky.

Treatment. Although the fungus inhabits the superficial layers of the epidermis, it is often resistant and difficult to eliminate. Attempts are made towards removal of the horny layer of the skin with daily baths of soap, preferably green soap, and warm water accompanied by mild friction with a soft loofa. Good results attend local application of salicylic acid, mercury, resorcin, sulphur, chrysarobin or combinations of these. Repeated painting of the spots with weak tincture of iodine is sometimes useful. The following prescriptions are suggested:

1. A 4 per cent solution of salicylic acid in absolute alcohol as a daily paint frequently effects a quick cure.

2. Epicarin, 3; salicylic acid, 6; white resorcin, 10; glycerin, 5; 80 per cent alcohol to 200 c.c.

3. Sodium hyposulphite lotion, 1 in 8, or sulphurous acid lotion, 1 in 4.

Lasting cures have been brought about in some cases by ultra-violet radiation and artificial sun therapy.

In conjunction with local treatment the discarding of tight-fitting and irritating underwear is essential. The personal precautions recommended under pinta are likewise applicable here, if not for the sake of contacts, at least to ensure destruction of as much of the organism as possible and to prevent possible auto-infection. Recrudescence may be avoided by perseverance with the treatment and the re-examination of the patient from time to time.

Pityriasis Flava
" Tinea Flava "

Definition. A common chronic tropical dermatomycosis producing patches ranging in colour between pale yellow and deep orange shades.

Aetiology, history and geographical distribution. In connection with the affection which he investigated in Ceylon, Castellani described the organism of pityriasis flava, *Malassezia tropica* (Castellani, 1905) Schmitter, 1923, from its appearance in the patches, but did not cultivate it. The disease is very common in all tropical countries, especially in Southern India and Ceylon, in the Malay States and in China. According to some authors tinea nigra is

synonymous with hodi-potsy, while others regard it as a variety of pityriasis versicolor.

Symptoms. The lesions affect principally the face, neck and trunk, and sometimes the extremities. They may first appear in early childhood in the form of tiny spots which grow and spread very slowly, the course of the disease extending over years with no likelihood of spontaneous cure. The patches are generally round or oval, but may assume practically any shape, rings, or bands connecting neighbouring spots may occasionally be found. The surface is smooth or covered with fine bran-like desquamations and on a level with the surrounding healthy parts. The basic colour is yellow, but various colours are met with, varying from pale yellow, canary-yellow, to deep orange. Confluence and spread of the lesions may ultimately implicate areas of extensive dimensions.

Natives constitute the majority of cases, but Europeans are not

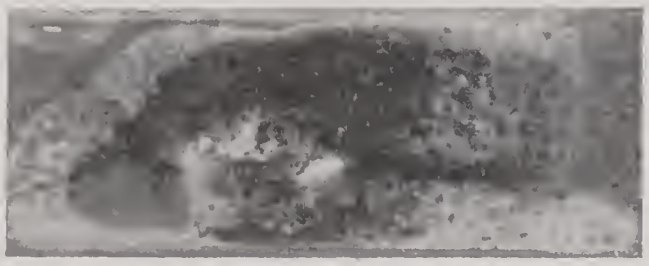

FIG. 122. *Malassezia tropica.* Culture on Sabouraud 2 per cent glucose-agar. (Original)

immune. The coloration of the spots on the latter is of a pinkish hue designated as *tinea rosea* and ascribed by Castellani to a different strain of *Malassezia tropica*. It is conceivable, however, that the respective normal skin pigmentation in dark and white individuals may have a bearing on the variety of colour produced. Tinea rosea is not to be confounded with "pityriasis rosea" (Gibert) an acute condition of unknown origin. No subjective symptoms or constitutional disturbances are observed, and pruritis is a rare complaint.

Diagnosis. In allied mycotic infections with similar patches the characters and distribution of the lesions, the immunity of certain parts of the body and the identity of the respective aetiological agents will help in the differential diagnosis. In recent lesions thick mycelial filaments with constrictions and irregularities in shape and diameter are seen, together with clusters of round or oval spores, 3·5–4·5μ in diameter. In more chronic cases the mycelium

and spores become comparatively rare, and the filaments assume even more irregular shapes and appear degenerated. The organism was not cultivated by Castellani.

A similar affection with discrete brown spots, areas of depigmentation and small vesicles at the edges of the lesions has been recorded by Weiss (1930). He was able to reproduce the infection by human inoculation with the parasite he isolated, *Aspergillus cinnamominus* (Weiss, 1930) Dodge, 1935.

Treatment. This infection is rather refractive to treatment, and apparent cure in cold weather, which is inimical to its existence, is often followed during the hot months by relapses, especially noticeable in Europeans returning home from the tropics. Local applications as for pityriasis versicolor are recommended and should be used over a prolonged period. Return of the patches to normal colour, although delayed after destruction of the fungus, eventually takes place.

Pityriasis Nigra
" Tinea nigra "

Definition. A dermatomycosis similar to pityriasis versicolor producing slightly desquamating black patches.

History, aetiology and geographical distribution. Manson (1872) described the same or a similar infection of the skin in China, and Castellani (1905) published another account of the disease in Ceylon and isolated the causative organism, *Dematium mansoni* (Castellani, 1905) Dodge, 1935 (synonym, *Cladosporium mansoni* Pinoy, 1912). It is of common occurrence in Ceylon and India, China and the Malay States.

Symptoms. Any part of the body may be affected with the exception of the palm and face, which are rarely implicated, and ordinarily the neck and anterior surface of the chest are the sites of election. The lesions take the form of non-pruritic more or less round patches, dull black in colour, isolated or confluent with slightly desquamating surfaces and are a little raised above the surrounding normal skin.

Europeans and natives are equally susceptible to infection. Some patients are occasionally seen in whom both the black patches of tinea nigra on the neck and the yellow ones of pityriasis flava on the face occur simultaneously. In this connection it may be mentioned that this polymorphism suggests pityriases versicolor, in fact some

authors consider tinea nigra and tinea flava as varieties of that disease.

Diagnosis. Clinically the condition should present no difficulty in being distinguished from other coloured mycotic or non-mycotic affections of the skin. Microscopically the parasite is found in abundance in scrapings of the patches in the epidermis as non-ramified, straight, bent or irregular hyphae, 18–20μ in length, and as groups of spores, 5–8μ in diameter, both elements containing dark pigment. Cultures, which are first green, then black, are hemispheric, rugose and are easily grown from the infected scales.

Treatment. This infection is quite amenable to treatment. There are instances in which a single application of pure formalin, especially on small patches, has cleared the lesion. This, however, should be performed with care. A 2 per cent lotion of salicylic acid in 80 per cent alcohol or a resorcin ointment ℥i to ℥i are also recommended. In order to effect a lasting cure the treatment has to be prolonged.

Pinta or Caratés

Definition. An obscure, probably mycotic and infectious affection provoking chronic inflammation and atrophy or dystrophy of the skin which assumes as a result various colours due to pigmentation, depigmentation and inflammation, varying in intensity in the diseased patches from white to red, blue, violet and almost black.

History and geographical distribution. The disease is very old-established in certain parts of the world, where it is curiously more or less limited in some endemic areas to river valleys, and reference to it exists dating as far back as 1760 in Mexico. Alibert (1829) described it under the name *taches endemique de Cordillères*, the Andes chain of mountains, and *pannus carateus*. Different local names for it are used by the natives of the respective endemic areas. It is common in the states of tropical America, especially in Colombia among the full-blooded negroes, in whom it was extensively studied by Montoya y Flores in 1893. The disease was first described in Brazil by Horta, and in 1891 Cerqueira investigated it in Bahia, but did not publish an account of his findings. It also occurs in Central America, the Antilles and the Philippine Islands. Various authors have reported it from Egypt (Madden and others), Libya and the Sahara (Legrain), the Malay States and China, and from the Gold Coast. The cases discovered in India and Ceylon are considered to be importations.

Aetiology. The mycotic nature of the affection was first recorded in 1879 by Sandoval in Mexico, but it is to Montoya y Flores that we owe our better conception of the disease as it exists in Colombia. He was able to discover mycelial filaments in scrapings of the epidermis and to obtain from them cultures belonging to different species. The actual inclusion, however, in sections of the skin in its deeper layers of hyphal elements, as seen by Gavino in Mexico and later by Gonzalez and Ochoterena, as well as by Chavarria and Shipley (1925) in Colombia, favours the mycotic theory.

Other writers at different times have formulated for the aetiology hypotheses of which may be mentioned the trophoneurotic, the chronic syphilitic or spirochaetal nature of the affection and bacterial agencies. It is noteworthy at this juncture that a significantly high Wassermann reaction index has been discovered among the patients in some endemic areas.

In a large percentage of cases of Pinta, *S. carateum*, a spirochaete similar to *Treponema pallidum*, was found by Alfonso, Triana and Blanco (1938) in Cuba in the Malpighian layers of the skin and in the superficial lymphatic glands. The organism is also demonstrable in the serum oozing after abrading the dyschromic areas, and was first described by Herrejon in 1927 as a probable cause of pinta.

On reviewing the mycotic and non-mycotic explanations and the arguments for and against, the result leaves the disease as obscure as ever, for fallacies could be picked in all of them. The fact that cultures are rarely obtained from the skin, which very often contains no mycelium on microscopic examination, coupled with the wide variety of species grown on successful occasions, seems to justify labelling these fungi as saprophytes, secondary organisms or normal inhabitants of the surface of the skin, or as the causative parasites of other dermatomycoses superimposed on, or wrongly diagnosed as pinta. On the other hand, there is one species, *Dematium wernecki* (P. Horta, 1921) Dodge, 1935 (synonym, *Cladosporium wernecki*), which is often isolated from black caraté in South America, and lesions have been reproduced by experimental inoculation in man, so until the contrary is proven the disease may be regarded as a true mycosis.

Among other fungi reported from cases of pinta, rightly named as such or otherwise, are species of *Acrothecium*, *Aspergillus*, *Penicillium* and allied genera, *Trichophytoneae*, some yeasts, as well as *Bacillus chromogenes caeruleus*.

Transmission. Here again the position is equally uncertain as the contradictory statements in their diversity tend to complicate rather than solve the problem. Insect vectors such as *Simulium ochraceum*, *S. haematopotum*, mosquitoes, bugs and even ticks have been suggested and incriminated. The epidemiology of the disease points to its contagiousness, denied by some on sufficiently good grounds, and altogether the subject remains debatable until indisputable proofs of one theory or another are forthcoming.

Symptoms. As the infection is practically unknown in infants it may be concluded that the incubation period is long. The patches which are characteristic of the disease are about 0·2–5 mm. in

FIG. 123. *Dematium* (*Cladosporium*) *wernecki*. Cultural morphology. 1. mycelium with chlamydospores, 2. mycelium with lateral conidia, 3. types of conidia. (Original)

diameter, becoming larger with age. They commence on the lateral and dorsal aspects of the fingers or the hand, the dorsum of the foot, on bony prominences, or on the face or some other exposed part of the body. Extension and coalescence of the patches in time affects practically the rest of the body with the exception of the palmar and plantar surfaces which are, nevertheless, hyperkeratinized, the genital regions, the gluteal folds, the nates and the flexures of joints. The scalp is sometimes attacked, the hairs turn white, thin out and eventually fall off, and nail involvement in the form of ridges occurs in some instances.

The spots are of different shapes, round, oval or with irregular borders, and assume the curious colours of white, red, blue, brown, black and other mixed hues. The white areas preponderate in chronic cases and are explained as cicatricial results of spontaneous

healing. One case may exhibit at the same time all the possible types of coloration.

Primarily, the lesions are usually brown and turn blue and black as they become older and more pigment is deposited in the cells of the epidermis and dermis. The hyperpigmented patches are gradually depigmented to the reddish tint which is due to a highly

FIG. 124. Pinta. *Dematium wernecki* isolated. (Original)

vascularized underlying area showing through a thinning epidermis. The red variety is the one met with in European patients. Scales on the surface, if at all present, are very fine and do not run to true desquamation and the level of the patch is seldom higher than the healthy neighbourhood. Pruritis, while admitted by some observers as a feature of the disease, is categorically denied by others. An interesting sign that could be elicited on the infected parts of the skin, especially where the spots are red, is that of dermographism when lines or words scratched with the nail or any blunt instrument induce

the elevation of wheals tracing the course of the scratches and going down slowly. The coloured spots show no impairment of function, sensory or otherwise, but the hairs on them often turn white and thin or disappear, due to fibrotic changes which have been noticed in their follicles.

Patients suffering from pinta develop in some cases cracked or ulcerated lesions with an offensive odour, which are considered to be sequels of trauma and secondary infection in the patches. The smell, though, may be attributed to a natural phenomenon of the excreted sweat being influenced by the type of food habitually consumed, aggravated by neglect of personal cleanliness. A high incidence of cardiac disease and some glandular swelling have been observed in the course of surveys of pinta patients, but it may be taken that the general health is not impaired and constitutional disturbances are non-existent. The principal complaint is the grotesque appearance the sufferer presents, leading in some patients to a state of intense depression and even suicide.

The disease is equally prevalent among both sexes, and no person of any age is immune except, perhaps, in early infancy. Individual hygiene and habits may act as barriers against infection, for Europeans and well-to-do negroes usually escape. The condition is generally less common in towns that it is in rural districts, and a high incidence of infection has been reported by Montoya y Flores among the miners of Colombia.

Contagion in crowded communities is recorded and some contacts have been known to develop lesions on the neck. Experimental transmission is claimed by Montoya and Uribe to have been effected in Colombia, but no definite rule could yet be laid regarding this possibility.

Indefinite duration in untreated cases is a peculiarity of the infection; some old patients give histories of the signs having first started in early childhood.

Diagnosis. This has to be accomplished on clinical and especially on endemic grounds. Microscopic examination of scrapings from the skin and cultures may be tried. Pityriasis versicolor is sometimes suspected but can be excluded by its distinctive distribution on the torso and that it leaves the hands and feet free, as well as by the presence of its causative species in the skin. Other dermatophytes and the parasite of tinea nigra can also be demonstrated in the epidermis on microscopical examination. In the scales, *D. wernecki* occurs as long, septate, straight or sinuous hyphae, rarely ramified,

with terminal arthrospores. Spores of variable size are occasionally aggregated in clumps. In bulk, hyphae are dark green.

Cultures of *D. wernecki* on varying media are produced in three types: *Dematium* with blastospores and abundant, humid yeast forms, *Cladosporium* with septate spores and *Fumago* with spherical, dark-coloured, thick-walled cells.

Non-mycotic affections producing loss or excessive deposition of pigment, for example, arsenical or lead-poisoning, Addison's disease, pellagra, tuberculosis, syphilis and malaria, are easily recognized by their respective symptomatologies and parasites. In leprosy, another possible source of error, the paraesthetic manifestations help in the diagnosis. Vitiligo, common as it is among the coloured races, presents a certain degree of difficulty in differential diagnosis. However, its distribution all over the body, in the skin folds and on the genital organs, together with the character of the spots, all white or pink, and their hyperpigmented borders should be enough for separating the two diseases. In *pityriasis rubra pilaris*, with which it may be confounded, the lesions appear as acuminate red papules, each with a broken hair in its centre and ringed by hyperkeratinization which extends into the hair follicle.

Treatment. The only therapeutic agents capable of giving satisfactory results, except in very chronic cases with depigmented lesions, are mercury, which has been employed since 1879 and was originally recommended by Sandoval, Neosalvarsan, or the alternate use of mercury and bismuth which are just as effective. The red areas seem to be the most favourably and quickly improved, but perseverance with the treatment is essential if lasting results are to be expected. Linimentum iodi, sulphur ointment or other fungicides may be employed externally. Frequent baths and change of underwear are necessary adjuncts to medical treatment. As a precautionary measure against possible contagion, personal linen should be boiled separately and only exclusively used by the patient.

Parasitic Achromia
" Hodi Potsy "

Definition. A mycotic affection of the epidermis inducing the formation of depigmented and scaly areas, principally on the skin of the face and neck.

History, aetiology and geographical distribution. The causative organism, *Hormodendron fontoynonti* Langeron, 1913, was

isolated by Fontoynont and Carougeau from the scales of a case of dermatomycosis in Madagascar where the affection is known as "hodi potsy." Jeanselme describes it as an *achromie parasitaire de la tête et du cou à récrudescence estivale.* The disease has been experimentally reproduced in man by the inoculation of a culture obtained from the epidermic scales.

FIG. 125. Parasitic achromia. *Endodermophyton roquettei* isolated. (Original)

Symptoms. Depigmented areas of irregular size and outline form on the skin of the face, neck and ears. They may exist in separate patches or merge into one another into big areas in which islands of normally-coloured skin can be seen. The surface is covered with fine scales which diminish in quantity or disappear during the cold season, only to reform with the advent of hot and damp weather. Subjective symptoms are practically non-exisent except, perhaps, for a slight pruritis in a few cases.

FIG. 126. *Hormodendron fontoynonti.* Cultural morphology. (After Langeron)

Diagnosis. The parasite exists in the scales in the form of short, sinuous hyphae, or as spherical spores congregated in clusters or isolated, some possessing one bud each. Its cultures, which grow easily, determine the diagnosis, and similar mycotic affections due to other species can at the same time be excluded. In vitiligo the patches are dead-white in colour, often possess a hyperpigmented outline and contain no fungus.

Mycelium in culture brown, septate, 2–7μ in diameter with dendritic sporophores. Blastospores are borne laterally on terminal conidiophores. End spores detach themselves from previously formed chains.

Treatment. A salicylic-resorcin ointment can be tried and persevered with for a long time. Dilute tinctura iodi mitis, 1 in 10, is also useful. Living in colder climes may eventually cure the condition.

Chimbéré

This refers to another parasitic achromia, an endemic dermatomycosis among the Indians along the Río San Miguel, Matto Grosso, Brazil, characterized by the production of confluent, circinate, desquamating, depigmented patches. The sites mostly affected are the face, neck and the anterior surface of the thorax. The lesions are found over areas ranging between 1 and 5 mm. in diameter, covered with easily detachable, colourless or white scales, while no abnormal pigmentation is met with elsewhere on the patient.

The causative organism, *Endodermophyton roquettei* Fonseca, 1925, can be isolated from the scales in which it occurs as ramified mycelium containing in some of its cells golden-yellow or dark reddish-brown granules. Successful human and animal inoculations are reported by Ota and Kawatsura (1931).

Colonies on ordinary media are moist, yellow or reddish and cerebriform.

For treatment a 4 per cent salicylic acid solution in absolute alcohol is often effective.

Tinea Albigena

History, aetiology and geographical distribution. Jeanselme reported this mycotic endemic disease from among the adult natives of Indo-China, and Nieuwenhuis isolated and described the causative agent from the nails of a Javanese. The parasite, *Aleurisma albiciscans* (Nieuwenhuis, 1908) Dodge, 1935, also occurs in Siam, the Malay Archipelago, and according to Castellani, occasionally in Ceylon.

Symptoms, diagnosis and treatment. The first stages are characterized by the production of pruriginous vesicles, 3–4 mm. in diameter, over the soles and palms, containing a yellowish fluid. In time they become purulent, break down, and finally dry up with accompanying hyperkeratinization, deep cracking and desquamation. The process, by slow extension and evolution, may ultimately come to include the leg or forearm, and invasion of the nails is a common

complication. The peculiarity of the affection lies in the depigmentation which eventually takes place in the involved areas.

Mycelium can be seen in detached portions of the skin and the cultures are slow of growth.

On Sabouraud agar, colony of *A. albiciscans* appears as an irregularly rounded disc, 4–6 cm. in 7 weeks, clear chamois in colour. On malt-agar coarse velvet with coremia. Good development on potato. Spores oval, 1–1·5μ in diameter, lateral, with or without pedicels. Intercalary spores 7–10μ in diameter, simple or irregularly branched conidiophores, aleurospores terminal or lateral, as a rule sessile and solitary, or in groups of 2 or 3.

The common fungicides, like chrysarobin ointment 5 per cent, iodine lotions, etc., bring about improvement or cure, but the affected parts do not regain their normal pigmentation.

Nodular Mycotic Affections of the Hair
Trichomycosis Axillaris

Definition. A nodular actinomycotic affection of the hairs of the axillary region due to infection with *Actinomyces tenuis* (Castellani, 1911) Dodge, 1935, either alone or in association with colour-producing micrococci.

Historical. Wilson (1898) described under the name "Leptothrix" a similar disease of the hair, also referred to as *trichomycosis palmellina* and *trichonocardiasis*, and later Castellani (1911) called attention to what seemed to be the same condition in natives and Europeans in the hot and damp districts of Ceylon. The affection has since proved to be more widespread and not confined to hot climates only. The causative fungus was named from its parasitic appearance in the hairs, but not cultivated until 1917 when Porcelli succeeded first in growing it. Other workers before him, in trying to obtain a culture of the fungus, were only rewarded with colonies of cocci, apparently existing in symbiosis with it. One other species, *Cryptococcus metaniger* Castellani, 1927, was isolated from a case of black trichomycosis.

Symptoms. The infected hair presents the appearance of a miniature string of minute beads, which in some cases are hardly visible to the naked eye, more or less equally spaced and similar in size. The concretions are easily scraped off the hair with a fine dissecting instrument, and may be yellow, black or, less commonly, red in colour.

On microscopical examination, the nodules are found to surround

the hair completely or only partially with varying degrees of thickness, singly or in the form of a confluent irregular sheath along parts of the shaft. Clearing agents and higher magnifications will reveal

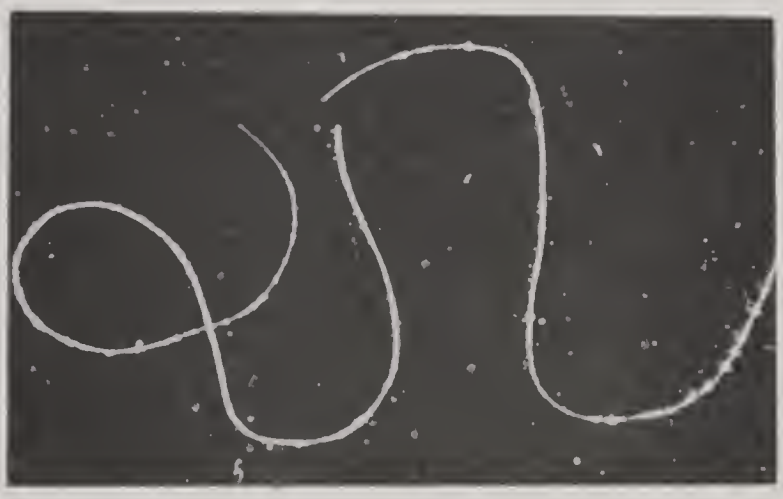

FIG. 127. *Trichomycosis axillaris.* Low magnification microphotograph of affected hairs on black background showing rosary disposition of nodules. (Original)

them as being composed of fine mycelial filaments, averaging 1μ or less in diameter, in short bacillus-like lengths, cemented together

FIG. 128. *Trichomycosis axillaris flava.* Note peeled cortex. (Original)

by a homogeneous substance. In tranverse sections, the fungus is seen to penetrate the hair deep into the medulla.

FIG. 129. *Trichomycosis axillaris rubra.* (Original)

The nodules owe their colour to the association with the fungus of *Micrococcus castellanii* Chalmers and O. Farrel, 1915, growing best on ordinary agar, in the red variety, and in the black forms, of

Micrococcus nigrescens Castallani, 1911, best grown on glucose-agar. The yellow variety is due to the fungus unaccompanied by bacteria.

Although the axillary hairs on one or both sides are those generally affected, the pubic hairs are sometimes the site of infection.

The course is chronic, and beyond the annoyance induced by being the subject of something abnormal and the staining of underclothing, the patient suffers no inconvenience, in fact the condition is invariably discovered by accident. Intermittent periods of amelioration or total disappearance in cold weather is a feature of the disease, especially noticed by Europeans who return home from tropical endemic areas.

Diagnosis. The presence of the coloured nodules on the axillary hairs is the main sign for the recognition of the disease. Microscopic examination and cultures on special media are essential for more accurate determination. Other conditions for which it might be mistaken have other distinctive features of site, aetiology, composition, etc., and will be dealt with next. Chromidrosis or coloured sweat, a similar affection, is not of fungous origin and produces no nodules.

Actinomyces tenius in its parasitic form occurs as delicate mycelial filaments about 0·7 — 0·8 μ in diameter, short, non-septate, usually unbranched, staining irregularly with Gram. A facultative anaerobe, it prefers relative anaerobiosis, and, while it does not grow on the usual media, it can be obtained in culture on blood or ascitic agar. On the latter, translucent colonies with a slightly opaque centre are formed.

Treatment. The disease is amenable to treatment with sulphur ointment, 1 in 10, and with disinfectant lotions. The affected hairs should be cut very short or better, shaved off. Nightly application of the ointment on retiring, and removing it in the morning with a warm antiseptic lotion give good results. Periodic examination for signs of recurrence is necessary, as the nodules tend to reappear on the hairs as soon as they attain an appreciable length.

Piedra and Trichosporosis

Definition. A nodular mycotic affection of the hairs due to infection with species of *Trichosporum* and *Piedraia*.

History, aetiology and geographical distribution. Originally well-recognized in Colombia where it is frequently met with, it also occurs in Argentina, Paraguay, Brazil, British and Dutch Guiana, Venezuela, as well as in Europe and Japan. The following tabulation

of the species responsible for the condition is in the chronological order in which most of the cases were recorded, and also includes the respective sites of infection:

Trichosporum beigelii (Rabenhorst, 1867) Vuillemin, 1902; Beigel's trichosporosis or tinea nodosa; moustache and beard; first reported from London.

T. ovoides Behrend, 1890; Behrend's trichosporosis or nodular trichomycosis; sycosis barbae; first recorded from Germany.

T. foxi Castellani, 1908; and

T. krusi Castellani, 1908; both reported by Castellani from India and Ceylon.

T. glycophile DuBois, 1910; DuBois' trichosporosis; vulval and pubic hairs of a diabetic patient.

T. ovale Paoli, 1913, non Unna ap. Vuillemin, 1902; Unna's trichosporosis or piedra nostras; moustache and beard.

Piedraia hortai (Brumpt, 1913) Fonseca and Arêa Leão, 1928; Brazilian piedra; discovered in 1911 by Horta in Rio de Janeiro.

P. sarmentoi Pereira, 1929; on the hairs of young adults; Rio Grande do Sul, Brazil.

P. venezuelensis Brumpt and Langeron, 1934; Caracas, Venezuela; not cultivated.

P. surinamensis Dodge, 1935.

P. colombiana Dodge, 1935 (= *Trichosporum giganteum* (Behrend, 1890) Vuillemin, 1902); Piedra of Colombia or trichosporosis tropica; scalp, beard and moustache.

Another species reported from Brazil, *Trichosporum equinum* Fambach teste Fonseca, 1930, produces white nodules which turn yellowish or a darker shade on the hairs of horses.

Symptoms and pathological appearances. The infected hairs are completely or only partially surrounded by the elements of the fungus in the form of nodules varying in diameter from microscopic dimensions to millimetres, or as more or less irregular sheaths with intervals of unaffected portions around the shaft of the hair.

In Brazilian piedra due to *Piedraia hortai* the nodules are black and hard, hence the name piedra or stone, adherent, few in number on each hair, and occur mainly on the scalp with a predilection for the longer hairs. The composition of the nodule is best conceived in transverse sections. It is constructed of a stroma of short, more or less parallel mycelial filaments, about 5μ in diameter, narrowly and irregularly septate, producing thereby the appearance of a mass of polygonal elements arranged at right angles to the longitudinal axis of the hair. The hyphae branch di- or trichotomously towards the periphery of the nodule, where they have the aspect of a fringe surrounding the mass. Included in the stroma, which is held together by some cementing interstitial substance, are fragments of the cuticular portion of the hair, as well as isolated or small groups

of asci borne at the tips of septate ascogenous hyphae. The ascus is ovoid, about 25μ in length, and encloses eight elongate, fusiform ascospores with a filiform appendage at each pole.

The fungus insinuates itself, after first penetrating the cuticular layer of the hair, and grows subcuticularly, more or less encircling the cortex without, however, attacking it, and finally, with further ramifications, the filaments escape back through the original perforations in the cuticle to encase that particular portion of the hair, and thus constitute the nodule.

Contrasted with the Brazilian type, the nodules in the piedra of Colombia caused by *Trichosporum giganteum* are smaller, lighter

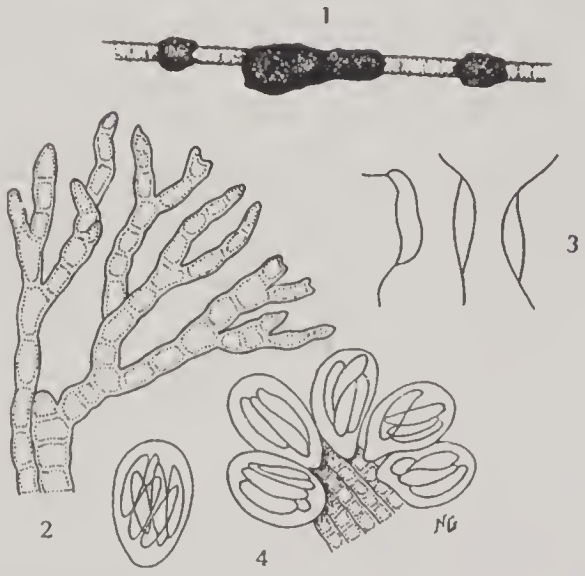

FIG. 130. *Piedraia hortai*. 1. infected hair, 2. filaments from edge of ascostroma 3. asci with filiform extremities (scolecospores), 4. asci with ascospores on septate filaments. (After Brumpt and Langeron)

in colour, resemble louse-nits and are not as strongly adherent to the hair. The fungus composing the nodule takes the form of polyhedral cells set in a mosaic pattern from mutual pressure. Each cell is about 2–10μ in diameter, the size getting bigger from the periphery of the mass towards the hair. Contrary to *P. hortai*, this species does not penetrate the cuticle but only surrounds it externally, and produces no asci or ascospores except in culture.

The nodules formed by *T. ovoides*, first discovered on the beard, are yellow in colour and the shaft of the hair remains unaffected by the fungus.

T. beigelii the cause of what was probably the first scientically recorded case of trichosporosis, occurs on the moustache and beard as nodules made up of cells, 3–4μ in diameter, irregularly compressed

into polygonal shapes and bound together by some form of gel. The cuticle of the hair is attacked, but only to a mild degree, by this species.

FIG. 131. *Piedraia colombiana* (= *Trichosporum giganteum*), culture on Sabouraud 2 per cent glucose-agar. (Original)

Of some interest is *T. glycophile* which was reported from the vulval hairs of a diabetic patient as causing pruritis, most probably due to the irritation of the sugar in the urine. The hairs, moistened with the glucose medium, presented permanently favourable conditions for the fungus to thrive. In this type of trichosporosis, mycelial filaments spread in between the fibrillae of the hairs, while the external layers of the nodules were composed of spore-like bodies.

Diagnosis. Correct diagnosis can only be arrived at by microscopical examination of cleared nodules and stained sections, as well as by cultural results.

On Sabouraud agar, *P. hortai* colonies are small, dark brown with lighter edges, very adherent, velvety, becoming black and folded. Hyphae septate, about 10μ in diameter, brownish. Ascospores indefinite in culture, fusiform, curved, each end acute and prolonged into an appendage about 30μ in length, the body of the spore about 30 × 10μ.

On the same medium, *P. colombiana* colonies cerebriform, non-adherent, at first white, then yellowish. Cells 5–8 × 5–12μ, yeast-like, forming a mycelium when older. Asci 50 × 30μ, containing eight 40 × 5–9μ, thick-walled ascospores with filiform, short appendages at either end.

FIG. 132. *P. colombiana*. Plate culture on Sabouraud 2 per cent glucose-agar. (Original)

Treatment. Whenever possible the hairs should be cut very short, shaved off, or regularly combed with a fine tooth-comb in the case of women, in order to get rid of as many nodules as possible. To counteract their hardness and tenacity and to ensure penetration of the ointment to be used, warmed antiseptic or soapy lotions or a 5 per cent solution of sodium bicarbonate are recommended. Unguentum hydrargyri ammoniati is quite effective.

CHAPTER XI

PITYRIASIS CAPITIS

Definition. A condition of universal and more or less obscure nature without apparent signs of inflammation or infection by the common ringworm parasites is recognized, variously explained and named by different observers. In the early stages of its development it is characterized by fine bran-like exfoliation of the epidermis of the scalp, the scales being coated with a variable amount of sebum. The commonest and popular name is "dandruff." *Pityriasis capitis*, suggesting the branny epidermal desquamation of the scalp, *seborrhoea capitis*, with increased secretion of sebum mixed with the detached scales, and other terms have been coined and are employed to describe this abnormality and the pathological changes induced during its course.

Aetiology and history. Originally discovered by Rivolta in 1873 in a case of psoriasis and named *Cryptococcus psoriasis*, the organism described from the lesions under discussion and incriminated in the infection has generally been labelled a yeast with varied generic and specific names. Malassez (1874) was the first to report it from the horny layer and follicular orifices in the scalp in cases of dry pityriasis, and he named it *Pitysporum*. Bizzozero (1884) renamed it *Saccharomyces ovalis*, which he changed in the same year to *S. sphericus*. In 1885 Oudemans and Peckelharing reported it from *seborrhoea capillitii*. Unna (1891) interpreted previous descriptions of the organism as relating to a flask-shaped bacillus "Flaschenbacillus," and was later supported in this view by Hoorn and others. The opinions about the nature of the organisms found at various times in the scalp lesions alternated between a bacillus and a yeast, and further taxonomic changes, assertions and contradictions were made by various workers, including Sabouraud, Vuillemin, and Castellani and Chalmers.

The present consensus of opinion, however, is in favour of Acton and Panja's species *Malassezia ovalis* (Bizzozero, 1884) Acton and Panja, 1927 as the causative agent, and that the other yeasts, bacilli and cocci incriminated by so many observers have either been the same organism first reported by Malassez or different stages in its

evolution. This species, together with the other representatives of the genus *Malassezia* Baillon, 1889, which produce different forms of pityriasis of the glabrous skin, and including the type species *M. furfur* of pityriasis versicolor, still remain rather obscure as to their true systematic position and relationship. The fact that they attack first the horny layer of the epidermis and sebaceous glands may indicate a dermatophytic affinity. On the other hand, the presence of yeast cells in the scales is suggestive.

As to whether the organism is of a specific nature in the production of the condition, there are contradictory reports from authoritative sources about its pathogenicity. Its isolation from the lesions in the scalp is no criterion when taken in connection with the facts of its occurrence in apparently normal scalps, in the mouth and in cerumen, and particularly its absence in many cases of true clinical pityriasis capitis. Ota and Huang (1933) consider it as an inoffensive saprophyte whose pathogenicity they failed to determine by intravenous and intraperitoneal animal inoculation, while its intradermic and subcutaneous injection only causes an evanescent erythema. Against these conclusions there is the claim of Moore (1934) who cultivated it on wort-agar and proved its pathogenic power.

Apart from the specific nature of *Malassezia* as an aetiologic agent or otherwise in pityriasis capitis and its sequela, which is mainly alopoecia, there are seemingly a few factors in the production of this latter condition which may be mentioned here. It is still debatable whether they act alone or in conjunction with *Malassezia* infection, predisposing to it or facilitating its progress as they are either based on scientifically insufficient and inconclusive data or merely the outcome of casual observation and lay theorization. They may be summarized in the following accounts, none of which can be considered as invariably tenable as causing the thinness and subsequent fall of hair and the irreversible alopoecia.

Heredity, endocrine or gonadal activity, high carbohydrate, fat or alcohol consumption, oily or alcoholic hair lotions, too frequent washing of the scalp or otherwise, warm, humid or dry atmospheres and, finally, the wearing or absence of a headgear are all blamed as determining factors. This is all irrespective of the recognized alopoecias of favus and *tinea tonsurans* and of the irritating drugs and methods employed in their treatment. There are also the alopoecias of non-mycotic bacterial infections as well as those of medical and surgical origin including the nervous, arthritic, syphilitic, post-typhoid, senile, cicatricial traumatic, etc.

It would seem, therefore, in the light of present-day accumulated knowledge, and until further more accurate data are available, that *Malassezia* may conveniently be retained, at least temporarily, as the aetiological agent in pityriasis capitis in its various forms, complications and sequelae as enumerated below under symptoms and pathological anatomy. At the same time, any suspiciously significant factor that may be associated with *Malassezia* or may be present without it, should always be borne in mind while arriving at a diagnosis and when treatment is attempted.

Morbid anatomy and symptoms. In the course of the first three years after birth, the superficial layer of the skin of the foetus (Rauber's layer) undergoes a normal and gradual keratinization. Failure of this process is followed by fatty degeneration and the eventual conversion of the whole layer into sebum. A superimposed infection by *Malassezia* tends to hasten the degeneration by interfering with the normal keratinization of the cells which desquamate as dandruff. The organism then invades the mouths of the hair follicles, extends deeply into them and attacks the pilo-sebaceous glands and, by irritating them, induces further production of sebum.

These pathological changes occur in various stages and vary in extent and degree during the different phases in the life of the individual, ranging from infancy to old age, and are not restricted to the scalp but spread to other areas of the body, producing further lesions which are often aggravated by secondary infection.

When *Malassezia* attacks the scalp during the early years of infancy, it becomes covered by a flat adherent greasy layer of scales, extensive or in patches, and of a dark brown colour from admixture with dirt. From the scalp, spread to the face results in mild pityriasiform, slightly erythematous lesions on the forehead, cheeks, behind the ears and on the back of the neck. Invasion of the pilo-sebaceous glands of the forehead and face produces papulo-vesicular eruptions due to blockage of the mouths of the glands while, occasionally, the sebaceous glands of the chest are affected and comedons are formed. Secondary invasion by streptococci leads to impetigenization of the lesions which are then liable to become distributed to any part of the body.

Between the periods of infancy and puberty, when the sebaceous and pilo-sebaceous glands are more or less inactive, further infections by *Malassezia* are less common until these glands begin to function anew.

From about the age of twelve, prior to puberty, and thereafter

during the phase of sexual maturation and active growth which usually stop when the age of twenty-five is attained, *Malassezia* is particularly evident on the scalp and causes the common dandruff. When it attacks the sebaceous glands, those of the nose, the naso-labial folds, the angles of the lips and a little below them towards the chin, the acne area on the face and the hat-band area (*corona seborrhoeica*), especially during the hot months, as well as those of the front of the chest and the interscapular region are liable to be affected.

FIG. 133. *Pityriasis capitis* simulating *tinea tonsurans*. (Original)

The scalp is covered completely or in parts with loose or easily detachable, white or greyish, bran-like scales, or the desquamating cells may remain adhering to the scalp in flat, more or less greasy flakes. From the scalp spread of infection causes *acne frontalis* on the forehead, blackheads and *acne vulgaris* on the nose and face respectively, as well as grouped comedons on the torso. Occasionally the eyebrows, eyelashes, beard and moustache may also be affected. Secondary pyogenic invasion of the sebaceous glands in these areas begins, if it takes place, as a papulo-vesicular erythematous rash which may develop into boils. The acne bacillus which may be

found in these lesions is in effect also a secondary invader thriving in the fatty plug of the infected and blocked sebaceous gland.

Later in life *Malassezia* shows a still greater tendency to attack, multiply in, and eventually destroy the hair follicles and sebaceous glands, the destructive process being hastened by secondary pyogenic invasion of the glands, follicles and shaft of the hair, and resulting in the familiar picture of alopoecia. The hairs become dry, lustreless, thin and distorted and, as their follicles and roots disappear, they fall off leaving ever-widening denuded areas of smoothly scarred, glazed and atrophic epidermis. This baldness (seborrhoeic alopoecia) may either start at the crown, on the forehead or simultaneously in both regions and, in the course of years, mysteriously enough only the temporal and occipital hairs are left unaffected.

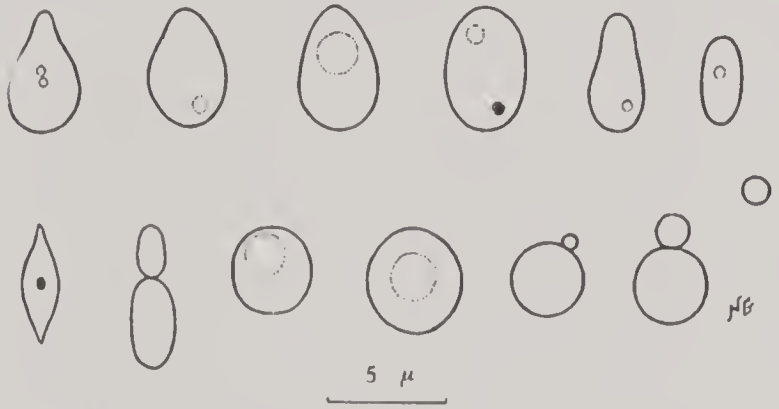

FIG. 134. *Malassezia ovalis.* Elements in "dandruff." (Original)

Moist folds of the skin, axillary and scrotal areas may also be involved with the usual sequence of changes occurring in the sebaceous glands, namely, blockage by multiplying *Malassezia*, retention of secretions, and accompanying secondary infection. Extension of *Malassezia* to these and other parts of the body is, however, of more common occurrence during the period of adolescence.

During old age the pent-up sebum in infected and blocked sebaceous glands leads to the formation of sebaceous cysts and seborrhoeic warts, and extension of *Malassezia* to glabrous areas of the skin usually gives a picture of exfoliative dermatitis and subsequent lichenification, especially in the popliteal and cubital flexures.

Diagnosis. *Malassezia ovalis* occurs in the scales as single or budding spherical or oval cells, thick- or thin-walled, about 3–10μ in diameter, with one or several oil droplets, the budding daughter

cell often producing with the mother cell the characteristic flask-shaped body. Delicate, irregular mycelial filaments, about 2–5μ in diameter and about 18μ in length are sometimes encountered.

Cultures of the organism are generally difficult to obtain and, if successful, the parasite does not survive transplantation. The best results, according to Ota and Huang, are attained on Petragnani's glucose-malachite green medium.

Emmons (1940) also obtained minute colonies of this yeast from infected scales as nuclei on acid (pH 5·5) dextrose broth with about 30 per cent glycerin to inhibit growth of contaminating bacteria. Being a lipophilic fungus, subcultures were successful on media prepared by pipetting ether extract of lanolin, oleic acid, or seborrhoeic scales over agar slants (Benham, 1939).

Treatment. This is generally disappointing. The best response is seen after the daily application of a lotion of weak tincture of iodine diluted ten times in 70 per cent alcohol. Coupled with the bactericidal and fungicidal effect of iodine any fresh deposit of parasites at the barber's ought to be avoided by thorough washing of the scalp at home after every haircut. The personal brush and comb must at the same time be washed as often as possible to get rid of accumulated scales containing the organism. In addition, any ascertainable or suggestive causes which may be present in a predisposing or directly active capacity should also receive due attention. The application of sulpha and penicillin ointments to deal with streptococci and staphylococci may be an essential adjunct in treatment.

CHAPTER XII

FUNGICIDES : FUNGISTATICS : PRESCRIPTIONS : MEDIA : POISONOUS FUNGI

Fungicides and Fungistatics

A collection of the commonly used fungicidal agents is given below for occasional reference. It is followed by a few prescriptions including some for application in non-mycotic skin infections which a mycologist cannot help encountering in his practice.

Inorganic Heavy Metals

Mercury

Unguentum Hydrargyri (blue ointment, 1 in 3), allays itching.

Ammoniated mercury

Unguentum Hydrargyri Ammoniati (white precipitate ointment, 10 per cent for fungicidal purposes), fungicide and parasiticide in sycosis and ringworm of the scalp and glabrous skin, as well as in their pyogenic complications, especially impetigo.

Nitrate of mercury

Unguentum Hydrargyri Nitratis (citrine ointment, 1 in 15), in granuloma of Majocchi, *tinea tonsurans* and complicating ulcers.

Perchloride of mercury (corrosive sublimate), 1–2 gr. to 1 oz. of water.

Lotio Hydrargyri Flava (yellow wash, 2 gr. to 1 oz.), both corrosive sublimate lotion and yellow wash for combatting pyogenic complications, eczema, loosening of crusts and alleviating pruritis in mycotic infections.

Subchloride of mercury (calomel)

Unguentum Hydrargyri Subchloridi (calomel ointment, 1 in 5), relieves itching and heals eczematous eruptions in *tinea marginata* and mycotic infection about the anus.

Lotio Hydrargyri Nigra (black wash, 3 gr. to 1 oz.), for pruritis.

Oleate of mercury

Unguentum Hydrargyri Oleati, 1 in 4, in *pityriasis versicolor*.

Oxides of mercury

Unguentum Hydrargyri Oxidi Flavi (golden ointment, 2 per cent) and

Unguentum Hydrargyri Oxidi Rubri (red precipitate ointment, 10 per cent), may be employed on occasions to suit bacterial secondary infections with impetigo in ringworm cases.

Manganese

Potassium permanganate, 1 in 1,000 is used as a warm bath in onychomycosis and in eczema and pustular or suppurating lesions complicating phytosis of hands and feet.

Lead

Lead subacetate

Liquor Plumbi Subacetatis Dilutus, 12·5 per cent of the strong solution, acts as an astringent and sedative and controls excessive discharge in weeping eczema complicating intertrigenous mycoses.

Lead iodide

Unguentum Plumbi Iodidi, 1 in 10, employed in *tinea circinata*.

Silver

Silver nitrate in 2 per cent solution may be painted with care over refractive tinea patches.

Zinc

Zinc carbonate

Lotio Calaminae has a soothing, astringent and drying effect in sycosis, *tinea marginata*, *tinea circinata*, etc.

Zinc oxide

Pasta Zinci Co. (Lassar's paste) and many other combinations has a sedative and healing effect in dysidrotic intertrigenous mycoses, some stages of eczematoid eruptions, as an emollient, etc.

Bismuth

Bismuth carbonate and

Bismuth subnitrate. Sedative astringent and antiseptic, included in dusting powders or ointments for intertrigenous mycoses and their eczematous complications. To be used on denuded surfaces as it does not penetrate the unbroken skin.

Iodine

Tinctura Iodi Mitis and *Tinctura Iodi Fortis*, the latter to be applied with great care and the former diluted five or more times to suit individual cases, while neither is to be used on raw surfaces undiluted. Universally useful in mycotic infections of the skin and its appendages.

Uguentum Iodi, 1 in 25, is employed for the same purposes. If the weak tincture or Linimentum iodidi (the strong tincture) prove too irritating, their excess may be removed with 70 per cent alcohol or eau de Cologne.

Lugol's Iodine solution (Pot. Iod., 2 gm.; Iodum, 1 vel 0·5 gm.; Aquae ad 100 c.c.) may be used as baths for onychomycosis or interdigital mycoses. Also for local injection around mycotic lesions, open or closed, into sinuses and fistulae and as a dressing. Useful in Madura foot.

Iodine preparations for intramuscular or intravenous injection in generalized and deep-seated lesions, in actinomycosis and maduromycosis as well as in refractive sycosis.

Potassium iodide. To be taken internally in massive doses, 10 gm. *per diem* in one litre of water in the absence of idiosyncrasy, and in conjunction with topical applications. Its free absorption by the body and subsequent elimination especially through the mucous membranes of the air passages, the urine and the skin, with the liberation of nascent iodine, make of it a valuable fungicide in deep-seated mycoses as well as in epidermophytosis.

Parasiticides

Sulphur

Sublimated sulphur

Unguentum Sulphuris, 1 in 10 and

Unguentum Sulphuris Co., Wilkinson's ointment, soft soap, 30; sublimed sulphur, 15; precipitated chalk, 10; tar, 15; lard, 30.

Precipitated Sulphur

Unguentum Sulphuris et Resorcini, precipitated sulphur, 4·5; resorcin, 3; yellow soft paraffin, to 100.

Sulphur ointments act as keratoplastics and fungicides, while the compound ointment is used in cases complicated by eczema and impetigo.

Icthyol is a useful fungicide, antiseptic and local anaesthetic. It promotes absorption of exudates and is incorporated in ointments in various strengths.

Boric acid. Warm 4 per cent lotions are used as fomentations for removal of crusts. The occasional wearing of socks soaked in the warm solution removes foetid odours in epidermophytosis of the feet with hyperiderosis. Included in dusting powders with zinc oxide and talc, it serves the same purpose.

Hydrogen peroxide solution is employed as a wash or bath in suppurative complications in phytosis.

Sulphurous acid. A lotion (2 dr. to 1 oz.) is sometimes used in ringworm.

Coal Tar Preparations
Disinfectants

Carbolic acid

Glycerinum Acidi Carbolici (1 in 5) is occasionally effective in ringworm of the scalp and pityriasis versicolor.

Pyrogallic acid. A tri-atomic phenol. Strong fungicide, parasiticide and antiseptic, employed with care in ringworm in ointment form (5 per cent) or in alcoholic solution (10 per cent) or combined with other fungicides.

Toxic symptoms. Gastro-intestinal disturbances, hypothermia, fainting, haemoglobinuria, black-coloured urine and death in a few days. In small amounts it colours the urine pink as it is eliminated with it.

Stains on linen are removable with ammonium persulphate rubbed in and then rinsed with water.

Creosote

Unguentum Creosoti (1 in 10) may be used on scaly mycoses and *tinea circinata.*

Beta-naphthol

Unguentum Naphtholis (Kaposi's ointment, 1 dr. to 1 oz.) acts as a fungicide on the scalp and glabrous skin. May be applied in alcoholic solution (2–3 per cent).

Epicarin. A beta-naphthol derivative used in ringworm as a 3–10 per cent alcoholic solution or in combination with other fungicides.

Formaldehyde solution. A 30 per cent strength in glycerine may be painted on patches of ringworm. Undiluted and very carefully applied, it may prove efficacious in depigmented mycotic lesions. A 10 per cent aqueous solution may be used.

Resorcin

Unguentum Resorcini, 1 in 8 and

Lotio Resorcini, 1 in 10. Incorporated in fungicidal ointments, resorcin acts as a stronger antiseptic than phenol and as an antipruritic.

Croton oil is a powerful local irritant. Has been used in ringworm of the scalp if the spots are discrete and small, but the risk of burning, followed by vesiculation, suppuration and ungainly scarring counterbalance its advantages.

Linimentum Crotonis, 1 in 8, may be tried instead of the pure oil.

Salicylic acid is a strong antiseptic and keratolytic; causes resolution of hyperkeratinization of the horny layer of the epidermis without much inflammatory reaction, and aids regeneration of new epithelium. It is incorporated in ointments and the keratolysis it induces lays bare mycelial elements to its fungicidal action and that of other included ingredients. It may also be applied in a 10 per cent alcoholic solution.

Benzoic acid is a superior antiseptic to salicylic and carbolic acids and is incorporated in fungicidal ointments, e.g. Whitfield's ointment.

Chrysarobin is effective as part of fungicidal ointments ($\frac{1}{2}$–10 per cent) or as a 10 per cent collodion.

Unguentum Chrysarobini, 1 in 25 or 10–15 gr. to 1 oz. of zinc oxide ointment.

Pigmentum Chrysarobini, chrysarobin, 1 dr.; chloroform, 10 dr.; pure gutta percha, 1 dr., may be painted on a patch of ringworm but not beyond it and covered with collodion.

Toxicity and contra-indications of chrysarobin. Fever, extensive erythema and haematuria have been noted among the toxic effects of absorption of the drug through the skin. It should not be applied on the face as it produces conjunctivitis and is also contra-indicated in renal insufficiency. If the tinea infection is extensive over a large surface of the body, chrysarobin should never be applied to more than one patch at a time. When that heals fresh areas may be treated to obviate

toxic absorption. The stains produced by the drug are removable with weak solutions of potash or chlorinated lime.

Volatile Oils

Rectified oil of turpentine in pure form may be tried with care as a paint over tinea patches.

Prepared coal tar

Liquor Carbonis Detergens is used in ointment form in chronic eczematous complications in phytosis.

Oil of cade is also employed in eczematous complications in liquid form, as an ointment, cereate or paint with collodion. Useful in obstinate pruritis.

Oil of cloves is recommended as an effective fungicide in *tinea circinata*.

Oil of cinnamon has the same action as oil of cloves.

Solid Volatile Oils

Thymol acts as a powerful antiseptic and is used in solution or other form in ringworm of the scalp and in sycosis.

Recently Recommended Fungicides

Iodolate (iodocholeate)
Cresatin (metacresyl acetate)
Merthiolate (1 : 10,000)
Sulphomerthiolate (1 : 1,000 powder)
Phenylmercuric nitrate tincture
Potassium mercuric iodide
Zephiran (a mixture of alkyl dimethyl-benzyl ammonium chloride)
Sodium propionate
Mersagel (phenyl mercuric acetate 1 : 750).
Sulpha preparations
Penicillin

Prescriptions

Whitfield.

℞

Acidi Salicylici		gr. xv
Acidi Benzoici		gr. xxv
Paraffini Mollis		℥ij
Olei Lavandulae		♏ iv
Olei Cocois	ad	℥j

Whitfield (*modified*).

R

Acidi Carbolici		gr. v
Acidi Salicylici		
Acidi Benzoici	āā	gr. xx
Vaselini	ad	℥j

Whitfield (*modified*).

R

Acidi Salicylici	2
Acidi Benzoici	4
Thymolis	1·4
Adepis Lanae Benz.	30

Interdigital mycosis.

R

Thymolis		gr. xx
Acidi Borici		℥ss.
Zinci Oxidi		
Pulveris Talci		
Zinci Stearatis	āā	℥ij

R

Sodii Thiosulphatis		
Thymolis Iodidi		
Acidi Borici	āā	ʒij
Lycopodii		
Pulveris Talci	āā	℥ij

Scalp and Glabrous Skin Mycoses.

R

Acidi Pyrogallici		gr. x
Sulphuris Praecipitati		ʒss.
Hydrargyri Ammoniati		gr. xv
Vaselini	ad	℥j

R

Pyrogallol		
Olei Cadini	āā	gr. xv
Vaselini	ad	℥j

R

Olei Cadini	10
Hydrargyri Oxidi Flavi	1
Vaselini	10
Lanolini	10

R

Chrysarobini		
Acidi Salicylici	āā	ʒi
Paraffini Mollis		℥ij

R

Bismuth Violet Crystals	1 gm.
Salicylic Acid	10 gm.
Alcohol 70 per cent to	100 c.c.

Pityriasis Versicolor.

R

Epicarini		3
Acidi Salicylici		6
Resorcini		10
Glycerini		5
Spiritûs Rectificati	ad	200

Pityriasis Capitis.

R

Resorcini		
Sulphuris Praecipitati	āā	gr. xx
Vaselini	ad	℥i

R

Acidi Salicylici		gr. x
Resorcini		ʒi
Vaselini	ad	℥j

Lassar's Paste.

R

Zinci Oxidi		
Pulveris Amyli	āā	ʒij
Acidi Salicylici		gr. x
Paraffini Mollis	ad	℥j

Media

Sabouraud's glucose and maltose media should only be employed for obtaining macroscopically determinable colonies of the dermatophytes. Glucose has a more deteriorating effect on cultures than dextrin or soluble starch. It is easily caramelized during sterilization which should, therefore, be shortened; otherwise development is retarded if not completely suppressed for lack of nutriment. In order to compensate for this short period of sterilization the glassware ought to be sterilized beforehand in the dry oven at 180° C. for at least an hour.

Maltose is equally spoilt by prolonged heat. It is hydrolized and fails to solidify on cooling. For these reasons, if the ingredients of a medium include glucose or maltose, the temperature during the process of solution should be brought up to 120° C. with only half the available heat of the autoclave. When this temperature is attained, the heat of the autoclave is turned off. After filtration and distribution in test-tubes these are sterilized in the same way.

Media for Cultivation of Dermatophytes

Ingredients	2 per cent glucose-agar	6 per cent glucose test medium	4 per cent maltose test medium	4 per cent Dextrin-agar	4 per cent soluble starch-agar	Conservation medium	Gorodkowa's poor medium
Lump glucose	20	60					10
Coarse maltose			40				
Dextrine				40			
Soluble Starch					40		
Granulated peptone	10	10	10	10	10	30	10
Agar	20	20	20	20	20	20	18
Water	1000	1000	1000	1000	1000	1000	1000

The addition of 30 gm. of agar instead of 20, and 20 gm. of peptone instead of 30 to the conservation medium obviates drying and reduces the number of transfers (Dodge).

Gorodkowa's medium is suitable for the development of asci. Its poverty in glucose makes the yeast exhaust the nutrient constituent in a short time and sporulation occurs for lack of nourishment. The medium must always be soft and humid.

Norris' Medium

For Actinomyces adjust *p*H to 7·4

Soluble Starch	2·0 gm.
Dipotassium Hydrogen Phosphate	0·2 gm.
Calcium Chloride	0·05 gm.
Ferric Chloride	0·01 gm.
Sodium Nitrate	0·06 gm.
Aspargin	0·05 gm.
Agar	20·0 gm.
Water to	1000 c.c.

Inspissated Loeffler's Glucose-Serum

For Actinomyces. Bouillon: Beef, 500 gm., add water to 1 litre. To this is added Peptone, 20 gm.; Sodium Chloride, 5 gm.; Glucose, 10 gm. One part of the mixture to be added to three parts of any animal serum. The medium needs no alkalinization. Slopes are inspissated at 70° to 75° C.

Macleod's Medium

For *Malassezia furfur*.

Agar	1·5 gm.
Peptone	2·0 gm.
Glycerol	2·0 gm.
Glacial Acetic Acid	1·0 m.
Distilled Water to	100 c.c.

Gentian violet 1 : 500,000 is a useful addition to restrain bacterial growth.

Raulin's Fluid

To purify strains of yeast-like fungi contaminated with bacteria. These are eliminated after one or two passages.

Candy Sugar	70·0 gm.
Tartaric Acid	4·0 gm.
Ammonium Nitrate	4·0 gm.
Ammonium Phosphate	0·60 gm.
Potassium Carbonate	0·60 gm.
Magnesium Carbonate	0·40 gm.
Ammonium Sulphate	0·25 gm.
Zinc Sulphate	0·07 gm.
Iron Sulphate (ferrous)	0·07 gm.
Potassium Silicate	0·07 gm.
Distilled Water to	1500 c.c.

Natural Media

Yeast Water

100 gm. of baker's yeast is boiled in a litre of water for 20 minutes, being stirred all the time. Leave to precipitate, decant, filter, put in test-tubes and autoclave at 120° C. for 15 minutes.

Potato Water

Wash a potato, peel, grate and weigh 20 gm. of pulp. Macerate for an hour in 1000 c.c. of water. Boil for five minutes, filter through cotton wool, put in test-tubes and autoclave at 120° C. for 15 minutes.

A poor medium, excellent for preserving cultures, for their purification and for bringing about filamentization and ascus formation of yeasts.

Potato or Yeast Water-Agar

These are made by the addition of 2 per cent agar to yeast or potato water.

Maize or Barley Flour Agar

Flour	40·0 gm.
Agar	20·0 gm.
Water to	1000 c.c.

Carrots and Potatoes

Wash, peel and cut up into convenient slices to fit test-tubes with water reservoir.

Grains of Cereals

A bed of cotton wool about 2 cm. deep is introduced into the bottom of the test-tube. The cotton wool is saturated with water, and a layer of grains of about the same depth is put on it. Autoclave at 120° C. for 20 minutes on two successive days.

Petroff's Egg Medium

Infuse 500 gm. of lean, finely-chopped beef in 500 c.c. of 15 per cent glycerine in water in refrigerator overnight. Squeeze through muslin a small amount at a time. To every 100 c.c. of infusion add 200 c.c. of well-beaten whole egg. Mix thoroughly and filter through muslin. Autoclave.

For *Malassezia* this medium is covered with 0·0004 per cent gentian violet to inhibit growth of staphylococci.

Chloral-Lactophenol Solution

For clearing scales and hairs instead of caustic potash

	by weight
Chloral Hydrate	2
Carbolic Acid (White Crystals)	1
Lactic Acid	1

Keep in amber-coloured bottle.

Poisonous Fungi

I. Toxic to smooth muscle fibres. Blood pressure raised:
Ergot of Rye (Pyrenomycetes, Hypocreaceae)—(*Claviceps purpurea*, Ergotin)

II. Haemolytic species:
Gyromitra esculenta (Ascomycetes, Pezizales), Helvellic Acid.

III. Emetico-cathartic fungi; toxins thermostable.
Lividian Syndrome.

IV. Fungi poisonous to nervous system:
A. Muscarian Syndrome.
B. Sudorine Syndrome.

V. Deadly fungi:
Phalloidean Syndrome.
Volva pustular, e.g., *Amanita muscaria*.
,, circumcised, e.g., *A. citrina*.
,, saccular, e.g., *A. phalloides*, *A. verna*, *A. irrosa*—deadly, *A. vaginata*—edible.

Lividian Syndrome

Entomola lividum
Genus Lactarius, *L. torminosus*.
Genus Russula, *R. emetica*.
Clytocybe olearia, (*C. cyathiformis*—edible).
Lepiota helviola.

Onset. After one to three hours.
Symptoms. Nausea, vomiting, diarrhoea, intense colic.
Course. Natural recovery in a day or two.

Muscarian Syndrome

Amanita muscaria, *A. pantherina*.

Mycoatropine poison of sympathetic nervous system, motor paralysis, vasodilatation, mydriasis, great prostration, deep cardiac depression.

Onset. One to two hours.
Symptoms. Gastro-intestinal disturbance without a respite, anuria, liver normal, cerebro-spinal irritation (muscarine drunkenness), convulsions, coma, death in 24 hours (2 per cent mortality) or recovery in a day or two.

Treatment. Emetics, diuretics, sedatives (chloral), cardiac stimulation (caffeine). No alcohol and especially no atropine.

Sudorine Syndrome

Clytocybe dealbata, Inocybe, Hebeloma.

Muscarine poison of the sympathetic, sudden cardiac failure.

Symptoms. Muscarian syndrome but more serious, hypersecretion of sweat and saliva, extreme bradycardia, cyanosis, myosis, depression.

Treatment. Atropine mainly.

Phalloidean Syndrome

Amanita phalloides, *A. verna*, *A. irrosa*.

Amanita haemolysin } destroyed at 65–70 degrees.
,, phalline }

,, toxin—nitrogen and sulphur, very stable, resists 100° C.

Cellular degeneration of liver and kidneys.

Onset. Ten to twenty hours or more.

Symptoms. Choleriform with occasional lulls, vomiting, diarrhoea, dehydration, thirst, anuria. Liver swollen and tender. Depression, ataxia, stupor.

Course. Delayed death, 3–10 days, 50 per cent mortality.

Treatment. Evacuation of stomach, rehydration, stimulants, antiphallinic serum (inoculation of horses with Amanita), administration of seven rabbits' brains and three stomachs (French method).

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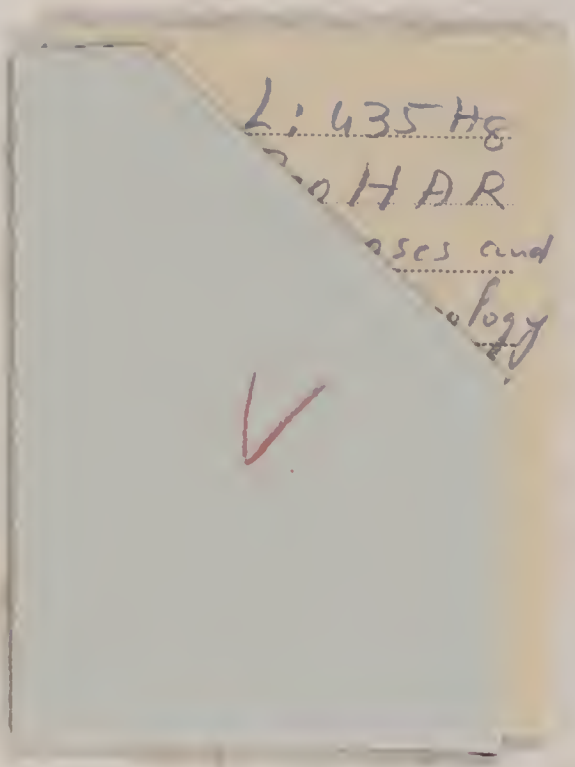
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